

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Exposure to heavy physical work from early to later adulthood and primary health care visits due to musculoskeletal diseases in midlife: a register linked study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-031564
Article Type:	Research
Date Submitted by the Author:	10-May-2019
Complete List of Authors:	<p>Halonen, Jaana; Finnish Institute of Occupational Health Shiri, Rahman; Finnish Institute of Occupational Health, Centre of Expertise for Health and Work Abili Mänty, Minna; University of Helsinki, Department of Public Health Sumanen, Hilla; South-Eastern Finland University of Applied Sciences, Health care and emergency care; University of Helsinki, Public Health Solovieva, Svetlana; Finnish Institute of Occupational Health, Center of Expertise for Health and workability Viikari-Juntura, Eira; Finnish Institute of Occupational Health, Kahonen, Mika; University of Tampere , Department of Clinical Physiology; Tampere University Hospital Lehtimäki, Terho Raitakari, Olli; University of Turku, Research Centre of Applied and Preventive Cardiovascular Medicine; Turku University Hospital, Department of Clinical Physiology and Nuclear Medicine Lallukka, Tea; Työterveyslaitos, ; Helsingin Yliopisto Laaketieteellinen tiedekunta, Department of Public Health</p>
Keywords:	Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, Physical work, Spine < ORTHOPAEDIC & TRAUMA SURGERY, Upper extremity, OCCUPATIONAL & INDUSTRIAL MEDICINE

SCHOLARONE™
Manuscripts

1
2
3 *Research article: BMJ Open*
4

5 Exposure to heavy physical work from early to later adulthood and primary
6 health care visits due to musculoskeletal diseases in midlife: a register linked
7
8 study
9
10
11
12

13 Jaana I. Halonen,¹ Rahman Shiri,¹ Minna Mänty,^{2,3} Hilla Sumanen,^{3,4} Svetlana Solovieva,¹

14 Eira Viikari-Juntura,¹ Mika Kähönen,⁵ Terho Lehtimäki,⁶ Olli T. Raitakari,^{7,8,9} Tea

15 Lallukka^{1,3}
16
17
18
19

20 1 Finnish Institute of Occupational Health, Helsinki, Finland

21 2 City of Vantaa, Finland

22 3 Department of Public Health, University of Helsinki, Helsinki, Finland

23 4 South-Eastern Finland University of Applied Sciences, Kotka, Finland

24 5 Department of Clinical Physiology, Tampere University Hospital, and Finnish
25 Cardiovascular Research Center - Tampere, Faculty of Medicine and Health Technology,
26 Tampere University, Tampere 33521, Finland

27 6 Department of Clinical Chemistry, Fimlab Laboratories, and Finnish Cardiovascular
28 Research Center - Tampere, Faculty of Medicine and Health Technology, Tampere
29 University, Tampere 33520, Finland

30 7 Centre for Population Health Research, University of Turku and Turku University Hospital,
31 Turku, Finland.

32 8 Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku,
33 Turku, Finland.

34 9 Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital,
35 Turku, Finland.
36
37
38
39
40

41 Corresponding author: Jaana I. Halonen, address: Finnish Institute of Occupational Health,
42 70032 TYÖTERVEYSLAITOS, Finland
43
44

45 E-mail: jaana.halonen@ttl.fi Telephone: +358 43 82 44 264
46
47
48
49

50 **Running title** Physical work from early to later adulthood and musculoskeletal visits
51
52

53 **Word count** 2437
54
55
56
57
58
59
60

Abstract (258/300)

Objectives: To examine whether exposure to heavy physical work from early to later adulthood is associated with primary health care visits due to cause-specific musculoskeletal diseases in midlife.

Design: Prospective cohort study

Setting: Nationally representative Young Finns Study cohort, Finland.

Participants: 1061 participants of the Young Finns Study cohort.

Exposure measure: Physical work exposure was surveyed in early (18–24 years old, 1986 or 1989) and later adulthood (2007 and 2011), and it was categorized as: “no exposure”, “early exposure only”, “later exposure only”, and “early and later exposure”.

Primary and secondary outcome measures: Visits due to any musculoskeletal disease and separately due to spine disorders, and upper extremity disorders were followed-up from national primary health care register from the date of the third survey in 2011 until 2014.

Results: Those with physically heavy work in early adulthood only had an increased risk of any musculoskeletal disease (risk ratio (RR) 1.55, 95% confidence interval (CI) 1.05–2.28) after adjustment for age, sex, smoking, body mass index, physical activity, and parental occupational class. Later exposure only was associated with visits due to any musculoskeletal disease (RR 1.46, 95% CI 1.01–2.12) and spine disorders (RR 2.40, 95% CI 1.41–4.06). Early and later exposure was associated with all three outcomes: RRs 1.99 (95% CI 1.44–2.77) for any musculoskeletal disease, 2.43 (95% CI 1.42–4.14) for spine disorders, and 3.97 (95% CI 1.86–8.46) for upper extremity disorders.

Conclusions: To reduce burden of musculoskeletal diseases, preventive actions to reduce exposure to or mitigate the consequences of physically heavy work throughout the work career are needed.

Key words: musculoskeletal; physical work; spine disorder; upper extremity

Strengths and limitations of this study

- We used self-reported assessment of physical heaviness of work that was based on a single question, which is why the specificity of the exposure, e.g. regarding exposure of different parts of the body, is low.
- We cannot rule out the possibility of changes in the exposure or outcomes between the survey waves.
- The setting enabled us to prospectively examine the long-term consequences of exposure to early and later physical work and midlife musculoskeletal health problems that were objectively measured.
- The used cohort data were representative of the general population with relatively little loss to follow-up.

Introduction

Musculoskeletal diseases (MSD) are the leading cause of work disability¹ measured as sickness absence² and disability retirements.³ In the European Union, the estimated total cost of lost productivity attributable to MSD among working-aged people can be up to 2% of gross domestic product (GDP).⁴ Contextual factors, particularly those related to workplace, have been identified as risk factors for sickness absence and disability retirement due to musculoskeletal problems^{5,6} as well as for musculoskeletal pain.⁷ We have reported findings where early and cumulative exposure to physical work were associated with low back pain at midlife.⁸ However, pain as an outcome is always self-reported, as well as a common condition. Thus, objective outcome measures are needed to confirm whether the effects of early and cumulative physical work are similar for more severe and objectively assessed MSD outcomes.

Only few studies to date have been able to assess the associations between cumulative exposure to physical work and MSD. A recent study used a job exposure matrix to assess exposure at the level of occupational title and disability retirement due to MSD,⁶ but even the first exposure measurements were mainly from midlife. In another study, two individual-level measurements were used to examine the associations between long-term exposure to high physical workload in midlife and risk of disability retirement due to MSD after age of 61,⁹ while younger employees were not included. Yet another study used individual-level physical work exposure data that were retrospectively assessed, and observed that cumulative exposure may increase the risk of sickness absence and disability retirement, but results for cause-specific outcomes were not reported.¹⁰ In addition to the lack of cumulative exposure data, prior studies have rarely accounted for family background although parental socioeconomic position has been linked, for example, to later musculoskeletal problems¹¹ and widespread pain.¹²

1
2
3 To fill these gaps in evidence, we examined whether physical heaviness of work
4
5 from early adulthood to later adulthood is associated with primary health care visits due to
6
7 MSD in midlife. Any MSD was examined as one outcome group, but we also included two
8
9 cause-specific groups: disorders of the spine and upper extremities. The contribution of
10
11 behavioural factors and parental socioeconomic position in these associations were
12
13
14 considered.

15 16 17 18 19 **Methods**

20 21 **Participants**

22
23 Data for this study are derived from the Young Finns Study.¹³ Cohort baseline data were
24
25 collected in 1980 in six age strata: 3, 6, 9, 12, 15, and 18 years resulting in 3596 participants
26
27 (response rate 83%). For this study, we included all those who were 18, 21 or 24 years when
28
29 responding to the survey in 1986 (wave 1). The wave 1 data were completed by including
30
31 also those who turned 18 years and responded to the survey in 1989 (**Figure 1**). The age-
32
33 based selection criterion was applied as the focus of this study was on early work-related
34
35 exposures. Further inclusion criterion required that the participants responded to the question
36
37 on physical heaviness of work in 1986 or 1989 (wave 1, early adulthood exposure), and in
38
39 2007 (wave 2, later adulthood exposure) and/or in 2011 (wave 3, later adulthood exposure),
40
41 which resulted in a total of 1170 participants. After excluding those with no follow-up or with
42
43 missing data on any covariate, the final study sample was 1170 cohort participants who all
44
45 had work exposure measurement from wave 1. Of these participants, 1023 had work
46
47 exposure data also from 2007, and 978 had work exposure data also from 2011. The study
48
49 has been ethically approved by the Ethics Committee of the Hospital District of Southwest
50
51 Finland.
52
53
54
55
56
57
58
59
60

Patient and Public Involvement statement

Patients or the public were not involved in the development of the research question or the design of this study nor in the conduct of the study.

Exposure

Physical heaviness of work was enquired at waves 1 to 3 with a single question: “How heavy is your work physically?”. There were six response alternatives: 1) light sedentary work, 2) other sedentary work, 3) physically light work, involving standing and moving, 4) medium heavy work involving moving, 5) physically heavy work, and 6) physically very heavy work. The responses were categorized as: sedentary/physically light work, and medium to heavy physical work. We used responses from all three waves to form a five-class exposure variable categorized as: “no exposure”, when reporting sedentary/physically light work in all three waves, “early exposure only”, when reporting medium to heavy physical work only in wave 1, “later exposure only”, when reporting medium to heavy physical work in waves 2 or 3 (89% responded to both waves 2 and 3), and “early and later exposure” when reporting medium to heavy physical work in wave 1 and in later adulthood in wave 2 and/or 3. All other possible response combinations formed a group “inconsistent exposure”.

Outcomes

We examined primary health care visits due to a musculoskeletal diagnosis. The follow-up started from the day after returning wave 3 survey in 2011, and continued until the first primary health care visit, death (from Statistics Finland) or end of the follow-up (end of 2014), whichever occurred first. Data were obtained from the register of primary health care visits (Avohilmo) maintained by National Institute for Health and Welfare.¹⁴ Diagnosis-specific data have been collected and were available from 2011 onwards. Visits due to *any*

1
2
3 *musculoskeletal diagnosis* by International Classification of Diseases (ICD) version 10 codes
4
5 M00-M99 were examined over the follow-up period. Additionally, two cause-specific
6
7 outcome groups with the largest numbers of events were: 1) disorders of the spine and 2)
8
9 upper extremity disorders. *Disorders of the spine* included any of the following diseases,
10
11 surgeries or treatments (ICD-10 code): cervical disc disorders (M50), lumbar and other
12
13 intervertebral disc disorders with radiculopathy (M51.1), other specified intervertebral disc
14
15 displacement (M51.2), disc degeneration (M51.3), disc disorders (M51.8), intervertebral disc
16
17 disorder, unspecified (M51.9), disc disorder/ disc disease (back disorders with radiation:
18
19 M50, M51), other dorsopathies (M53), back pain / dorsalgia (back disorders without
20
21 radiation: M54.1, M54.2, M54.3, M54.4, M54.5, M54.6, M54.8, M54.9), and lumbar disc
22
23 herniation or sciatica (M51.1, M51.2, M54.3, and M54.4). *Upper extremity disorders*
24
25 included any of the following diseases, surgeries or treatments: carpal tunnel syndrome,
26
27 carpal tunnel release (G56.0, ACC51, ACC59), shoulder disorder (M75), medial
28
29 epicondylitis, lateral epicondylitis, and periarthrititis of wrist (M77.0, M77.1, M77.2, or
30
31 M77.3). Additionally, the numbers of visits due to osteoarthritis (M15, M16, M17, M18)
32
33 were examined, but found to be too low for statistical analyses (see Table 1).
34
35
36
37
38
39
40
41
42

43 Covariates

44 From the questionnaires we obtained information on possible confounders. We included sex
45
46 and age at wave 1, and parental occupational status in childhood (1=upper non-manual,
47
48 2=lower non-manual, 3=upper manual, 4=lower manual). Smoking (ever smoker vs. non-
49
50 smoker) and body mass index (BMI, kg/m² based on measured weight and height) were
51
52 included as time varying covariates collected at baseline, 2001, 2007 and 2011. Measure for
53
54 physical activity (PA) was based on a set of questions requesting the frequency and intensity
55
56 of PA, frequency of vigorous PA, hours spent on vigorous PA, average duration of a PA
57
58
59
60

1
2
3 session, and participation in organized PA. Based on these questions a *physical activity index*
4 was calculated (range 5-15, larger value indicating greater activity).¹⁵ For PA, we used the
5 maximum of the three measurements of the PA index in adulthood (2001, 2007 and 2011), as
6 these data had plenty of missing values, but the patterns of PA have been observed to remain
7 constant in adulthood.¹⁶ Missing data on covariates were imputed using mean of the study
8 sample in the corresponding survey. All these covariates have been linked to back problems
9 in prior studies.^{11 17-19}

21 Statistical analyses

22 We used generalized estimating equation models with Poisson distribution to assess
23 associations between the five-class physical work exposure, “no exposure” serving as the
24 reference group, and primary health care visits due to MSD. We ran models separately for all
25 musculoskeletal visits, for disorders of the spine, and for upper extremity disorders. Two
26 model specifications were used: Model 1 was adjusted for sex and age at baseline, Model 2
27 was additionally adjusted for parental occupational class and time-varying smoking, BMI and
28 physical activity. Results are presented as risk ratios (RR) with 95% confidence intervals
29 (CI). As an alternative method, we ran the analyses using Cox proportional models, which
30 resulted in very similar findings (data not shown).

47 Results

48 Descriptive statistics of the analysis sample in total and by sex are shown in Table 1. At
49 baseline, mean age was 20.5 (SD=2.9) years, and mean BMI 22.4 (SD=2.3), while the mean
50 BMI during the follow-up was 25.5 (SD=4.8). Mean follow-up time for first visits due to any
51 MSD was 3.2 (SD=0.87) years, due to spine disorders 3.4 (SD=0.63) years, and due to upper
52 extremity disorders 3.4 (SD=0.50) years. Distributions of the outcomes and proportions of
53
54
55
56
57
58
59
60

1
2
3 events in each of the five exposure groups in total and by sex are presented in Table 2. As
4
5 shown in Table 2, the low numbers of events prevented sex-specific analyses.
6
7

8 Associations between physical heaviness of work and primary health care visits
9
10 due to the three outcome groups are presented in Table 3. Overall, the age- and sex-adjusted
11
12 estimates (Model 1) were slightly attenuated after including parental occupational status
13
14 smoking, BMI and physical activity (Model 2). We observed an association between early
15
16 exposure only and any musculoskeletal disorders (fully adjusted RR 1.55, 95% CI 1.05–2.28)
17
18 and a slightly weaker association for later exposure only (RR 1.46, 95% 1.01–2.12). Early
19
20 and later exposure had the strongest association with any visits due to MSD (RR 1.99, 95%
21
22 CI 1.44–2.77).
23
24
25

26 For disorders of the spine, we observed an association for later exposure only
27
28 (RR 2.40, 95% CI 1.41–4.06), inconsistent exposure (RR 2.30, 95% CI 1.34–3.95), and early
29
30 and later exposure (RR 2.43, 95% CI 1.42–4.14). Effect estimates for visits due to upper
31
32 extremity disorders were also positive, that for early and later exposure (HR 3.97, 95% CI
33
34 1.86–8.46) reaching statistical significance, although with a wide confidence interval.
35
36
37
38
39

40 Discussion

41
42 In this study, reporting both early and later exposure to heavy physical work was associated
43
44 with objectively measured MSDs requiring primary health care visit in midlife. In addition,
45
46 physical heaviness of work in early adulthood only was associated with an increased risk of
47
48 primary health care visit due to any MSD, and exposure in later adulthood only was
49
50 associated with any MSD and disorders of the spine. These diagnosis-specific findings are in
51
52 line with our prior findings for self-reported low back pain.⁸ Although our current analyses
53
54 may have lacked power to detect precise associations, particularly for upper extremity
55
56 disorders, the findings suggest that physical work exposure is also a predictor of objectively
57
58
59
60

1
2
3 measured MSDs even after considering behavioural factors and parental socioeconomic
4
5 position.
6

7
8 Longitudinal studies on the associations between physical work exposures and
9
10 objectively measured MSDs are scarce. Specifically, we are not aware of studies that would
11
12 have collected and used data on work-related physical exposures of participants from early to
13
14 later adulthood, and health care visits due to MSDs in midlife. Some evidence exists
15
16 regarding physical work exposures and musculoskeletal pain or disorders at an early stage of
17
18 the working career. In one cross-sectional study repetitive and asymmetric demands,
19
20 including high probability of repetitive tasks, bending or rotation movements and manual
21
22 materials handling, was associated with the presence of neck/shoulder pain and severity of
23
24 upper- and lower-back pain among 21-year-old employees.²⁰ Another cross-sectional study
25
26 among less than 30-year-old employees reported similar results regarding the association
27
28 between physical work exposures (e.g. repetitive flexion or rotation movements of the trunk,
29
30 and more than three years in a job including lifting more than 25 kg at least once an hour) and
31
32 low back pain.²¹ However, in these studies follow-up for mid-life musculoskeletal disorders
33
34 was not available. Timing of outcome measurement seems essential as it is likely that there
35
36 are differences in associations between physical work and MSD among 20-35, 36-49 and
37
38 over 50-year old employees.²²
39
40
41
42
43

44
45 Several studies have reported associations between physical work exposures
46
47 and increased risk of objectively measured disability retirement due to MSD.^{5 23-25} However,
48
49 only one of these studies examined how exposure in early adulthood was associated with
50
51 disability retirement due to MSD in mid-life.²⁵ Moreover, only a few studies have reported
52
53 associations between cumulative exposure to physical work throughout the work career and
54
55 objectively measured sickness absence or disability retirement in general,²⁶ or due to
56
57 disability retirement due to MSD in particular.⁶ These findings have been in line with ours,
58
59
60

1
2
3 although the cumulative exposure in the study focusing on MSD was assessed using a job
4 exposure matrix.
5
6

7
8 Some limitations of this study need to be acknowledged. We used self-reported
9 assessment of physical heaviness of work that was based on a single question. Consequently,
10 the specificity of the exposure, e.g. regarding exposure of different parts of the body, is low.
11
12 Although such questions have widely been used in epidemiological studies and have
13 indicated good validity,²⁷ this may partly explain the non-significant associations between
14 physical work and upper extremity disorders. We cannot rule out the possibility of changes in
15 the exposure or outcomes between the survey waves, however, the long follow-up enabled us
16 to examine the long-term consequences of early and later physical work and midlife
17 musculoskeletal health problems that were objectively measured. It can be speculated that
18 primary health care visits with musculoskeletal diagnosis among the middle aged are mostly
19 a result of pain complaints. Severe pain may interfere with work activities and induce need
20 for sickness absence, which may be the primary motivation for the visit to a physician. Thus,
21 the used outcomes may reflect the severity of work disability due to musculoskeletal pain.
22
23 The follow-up period for the outcomes was neither very long; however, the major strength of
24 this work is the prospective study design with three repeated assessments of physical
25 heaviness of work that were initiated already in early adulthood. Moreover, the used cohort
26 data were representative of the general population with relatively little loss to follow-up.¹³
27
28 This suggests good generalizability to the Finnish working population, while more caution is
29 needed when assessing generalizability to other countries with different health care systems.
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50

51 In summary, our findings suggest that exposure to heavy physical work over the
52 work career contributes to the high burden in the health care. Therefore, preventive actions
53 against musculoskeletal problems due to physically heavy work in early adulthood, later
54 adulthood and cumulatively throughout the work career are needed. One possible action,
55
56
57
58
59
60

1
2
3 specifically among young employees, might be good introduction to ergonomic ways to
4
5 work. Guidance on how to recover from physical work tasks is also important; for example,
6
7 at individual level recovery training has been seen beneficial to the employees.²⁸ At
8
9 organizational level, procedures enabling recovery during the work day could include task
10
11 variation and convenient work-break schedules,²⁸ which are likely to be applicable
12
13 throughout the work career.
14
15

16 17 18 19 **A competing interest declaration**

20
21 All authors have completed the Unified Competing Interest form at
22
23 www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and
24
25 declare that (1) JIH and TLa have support from the Academy of Finland; (2) JIH and TLa
26
27 have no relationships with the Finnish Academy that might have an interest in the submitted
28
29 work in the previous 3 years; (3) their spouses, partners, or children have no financial
30
31 relationships that may be relevant to the submitted work; and (4) JIH, RS, HS, MM, SS, EV-
32
33 J, MK, TLe, OR and TLa have no non-financial interests that may be relevant to the
34
35 submitted work.
36
37
38
39
40
41

42
43 **Authors' contributions** JIH, RS, MM, HS, EV-J, SS and TLa conceived and designed the
44
45 experiments, TLa analysed the data, JIH wrote the first draft of the article, MK, TLe and OR
46
47 contributed materials and/or analysis tools. TLa, MK, TLe and OR contributed to the funding
48
49 of the study. TLa is the guarantor of the study. All authors were involved in interpretation of
50
51 the findings, writing the paper and approved the submitted and published versions.
52
53
54
55

56
57 **Funding** The research was funded by the Finnish Academy (grant numbers 287488 and
58
59 319200 for TLa and JIH). The Young Finns Study has been financially supported by the
60

1
2
3 Academy of Finland: grants 286284, 134309 (Eye), 126925, 121584, 124282, 129364,
4
5 129378 (Salve), 117787 (Gendi), and 41071 (Skidi); the Social Insurance Institution of
6
7 Finland; Competitive State Research Financing of the Expert Responsibility area of Kuopio,
8
9 Tampere and Turku University Hospitals (grant X51001); Juho Vainio Foundation; Paavo
10
11 Nurmi Foundation; Finnish Foundation for Cardiovascular Research; Finnish Cultural
12
13 Foundation; The Sigrid Juselius Foundation; Tampere Tuberculosis Foundation; Emil
14
15 Aaltonen Foundation; Yrjö Jahnsson Foundation; Signe and Ane Gyllenberg Foundation;
16
17 Diabetes Research Foundation of Finnish Diabetes Association; and EU Horizon 2020 (grant
18
19 755320 for TAXINOMISIS); and European Research Council (grant 742927 for
20
21 MULTIEPIGEN project); Tampere University Hospital Supporting Foundation.
22
23
24
25
26
27

28 **Ethics approval** The study has received ethical approval from the Ethics Committee of the
29
30 Hospital District of Southwest Finland on September 21st, 2010.
31
32
33
34

35 **Data sharing** No additional data available
36
37
38
39

40 **Acknowledgements** The authors thank statistician Niina Kartiosuo for her help with the
41
42 formation of the analysis dataset.
43
44
45
46

47 **Figure Legend**

48
49 **Figure 1.** Study design.
50
51
52
53
54
55
56
57
58
59
60

References

- 1 OECD. *Sickness, Disability and Work: Breaking the Barriers. A Synthesis of Findings across OECD Countries* OECD Publishing, Paris. 2010.
- 2 Linaker C, Harris EC, Cooper C, Coggon D, Palmer KT. The burden of sickness absence from musculoskeletal causes in Great Britain. *Occup Med (Lond)* 2011;61:458-64.
- 3 Statistics Finland. *Recipients of disability pension 2018*.
- 4 Bevan S. Economic impact of musculoskeletal disorders (MSDs) on work in Europe. *Best Pract Res Clin Rheumatol* 2015;29:356-73.
- 5 Foss L, Gravseth HM, Kristensen P et al. The impact of workplace risk factors on long-term musculoskeletal sickness absence: a registry-based 5-year follow-up from the Oslo health study. *J Occup Environ Med* 2011;53:1478-82.
- 6 Ervasti J, Pietilainen O, Rahkonen O et al. Long-term exposure to heavy physical work, disability pension due to musculoskeletal disorders and all-cause mortality: 20-year follow-up-introducing Helsinki Health Study job exposure matrix. *Int Arch Occup Environ Health* 2018.
- 7 Madsen IEH, Gupta N, Budtz-Jorgensen E et al. Physical work demands and psychosocial working conditions as predictors of musculoskeletal pain: a cohort study comparing self-reported and job exposure matrix measurements. *Occup Environ Med* 2018;75:752-758.
- 8 Lallukka T, Viikari-Juntura E, Viikari J et al. Early work-related physical exposures and low back pain in midlife: the Cardiovascular Risk in Young Finns Study. *Occup Environ Med* 2017;74:163-168.
- 9 Kjellberg K, Lundin A, Falkstedt D, Allebeck P, Hemmingsson T. Long-term physical workload in middle age and disability pension in men and women: a follow-up study of Swedish cohorts. *Int Arch Occup Environ Health* 2016;89:1239-1250.
- 10 Sundstrup E, Hansen AM, Mortensen EL et al. Retrospectively assessed physical work environment during working life and risk of sickness absence and labour market exit among older workers. *Occup Environ Med* 2018;75:114-123.
- 11 Lallukka T, Viikari-Juntura E, Raitakari OT et al. Childhood and adult socio-economic position and social mobility as determinants of low back pain outcomes. *Eur J Pain* 2014;18:128-38.
- 12 Power C, Atherton K, Strachan DP et al. Life-course influences on health in British adults: effects of socio-economic position in childhood and adulthood. *Int J Epidemiol* 2007;36:532-9.
- 13 Raitakari OT, Juonala M, Ronnema T et al. Cohort profile: the cardiovascular risk in Young Finns Study. *Int J Epidemiol* 2008;37:1220-6.
- 14 National Institute for Health and Welfare. *Register of Primary Health Care visits, Helsinki: National Institute for Health and Welfare 2019*.
- 15 Rovio SP, Yang X, Kankaanpaa A et al. Longitudinal physical activity trajectories from childhood to adulthood and their determinants: The Young Finns Study. *Scand J Med Sci Sports* 2018;28:1073-1083.
- 16 Telama R, Yang X, Leskinen E et al. Tracking of physical activity from early childhood through youth into adulthood. *Med Sci Sports Exerc* 2014;46:955-62.
- 17 Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between smoking and low back pain: a meta-analysis. *Am J Med* 2010;123:87.e7-35.
- 18 -. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol* 2010;171:135-54.
- 19 Shiri R, Euro U, Heliovaara M et al. Lifestyle Risk Factors Increase the Risk of Hospitalization for Sciatica: Findings of Four Prospective Cohort Studies. *Am J Med* 2017;130:1408-1414.e6.
- 20 Lourenco S, Araujo F, Severo M, Cunha Miranda L, Carnide F, Lucas R. Patterns of biomechanical demands are associated with musculoskeletal pain in the beginning of professional life: a population-based study. *Scand J Work Environ Health* 2015;41:234-46.

- 1
2
3 21 Van Nieuwenhuysse A, Fatkhutdinova L, Verbeke G et al. Risk factors for first-ever low back
4 pain among workers in their first employment. *Occup Med (Lond)* 2004;54:513-9.
5 22 Oakman J, Neupane S, Nygard CH. Does age matter in predicting musculoskeletal disorder
6 risk? An analysis of workplace predictors over 4 years. *Int Arch Occup Environ Health*
7 2016;89:1127-36.
8 23 Lahelma E, Laaksonen M, Lallukka T et al. Working conditions as risk factors for disability
9 retirement: a longitudinal register linkage study. *BMC Public Health* 2012;12:309.
10 24 Robroek SJW, Jarvholm B, van der Beek AJ, Proper KI, Wahlstrom J, Burdorf A. Influence of
11 obesity and physical workload on disability benefits among construction workers followed
12 up for 37 years. *Occup Environ Med* 2017;74:621-627.
13 25 Ropponen A, Svedberg P, Koskenvuo M, Silventoinen K, Kaprio J. Physical work load and
14 psychological stress of daily activities as predictors of disability pension due to
15 musculoskeletal disorders. *Scand J Public Health* 2014;42:370-6.
16 26 Sundstrup E, Hansen AM, Mortensen EL et al. Cumulative occupational mechanical
17 exposures during working life and risk of sickness absence and disability pension:
18 prospective cohort study. *Scand J Work Environ Health* 2017;43:415-425.
19 27 Stock SR, Fernandes R, Delisle A, Vezina N. Reproducibility and validity of workers' self-
20 reports of physical work demands. *Scand J Work Environ Health* 2005;31:409-37.
21 28 Verbeek J, Ruotsalainen J, Laitinen J et al. Interventions to enhance recovery in healthy
22 workers; a scoping review. *Occup Med (Lond)* 2018.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1. Descriptive statistics of the study population at baseline, percentages (%).

Variable (N missing)	All	Men	Women
	N _{obs} =5850 %	N _{obs} =2490 %	N _{obs} =3360 %
Parental occupational status (125)			
upper non-manual	14	15	14
lower non-manual	42	40	44
upper manual	27	28	26
lower manual	17	17	16
Ever smokers (-)	46	51	46
Low physical activity index* (30)	67	67	67
Cumulative exposure to heavy physical work (-)			
No exposure	49	37	58
Early exposure only	12	16	8
Later exposure only	13	10	15
Inconsistent exposure	11	11	11
Early and later exposure	15	26	8
Outcomes (-)			
Any musculoskeletal disease	21	17	24
Disorders of the spine	10	8	11
Upper extremity disorders	5	4	6
Osteoarthritis	1.4	0.8	1.8

* Index score 5-10

Table 2. Number of observations and proportions (%) of primary health care visits due to musculoskeletal diseases by the exposure categories for physical heaviness of work between 2011 and 2014.

Physical heaviness of work	Any musculoskeletal disease N _{obs} (%)	Disorders of the spine N _{obs} (%)	Upper extremity disorders N _{obs} (%)	Osteoarthritis N _{obs} (%)
All	1120	540	265	80
No exposure	420 (37)	175 (32)	70 (26)	45 (0.8)
Early exposure	140 (12)	65 (12)	35 (13)	20 (0.4)
Later exposure	165 (15)	105 (19)	45 (17)	5 (0.1)
Inconsistent exposure	175 (16)	85 (16)	35 (13)	10 (0.2)
Early and later exposure	220 (20)	110 (20)	80 (30)	0 (0)
Men	745	360	170	60
No exposure	340 (46)	105 (42)	50 (29)	35 (58)
Early exposure	60 (8)	30 (8)	15 (9)	15 (25)
Later exposure	110 (15)	65 (18)	30 (18)	5 (8)
Inconsistent exposure	130 (18)	55 (15)	35 (21)	5 (8)
Early and later exposure	105 (14)	60 (17)	40 (23)	0 (0)
Women	375	180	95	20
No exposure	80 (21)	25 (14)	20 (21)	10 (50)
Early exposure	80 (21)	35 (19)	20 (21)	5 (25)
Later exposure	55 (15)	40 (22)	15 (16)	0 (0)
Inconsistent exposure	45 (12)	30 (17)	0 (0)	5 (25)
Early and later exposure	115 (31)	50 (28)	40 (42)	0 (0)

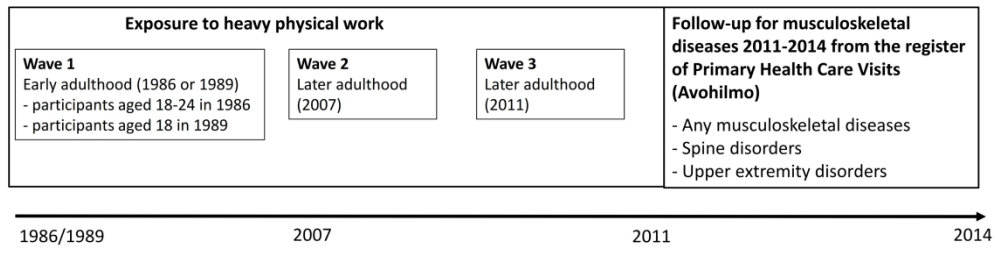
Table 3. Risk ratios for primary health care visits due to musculoskeletal diseases in relation to early and later exposure to heavy physical work.

Physical heaviness of work	Model 1*			Model 2†		
	RR	95% CI		RR	95% CI	
<i>Any musculoskeletal disease</i>						
No exposure	1			1		
Early exposure	1.65	1.12	2.41	1.55	1.05	2.28
Later exposure	1.55	1.08	2.22	1.46	1.01	2.12
Inconsistent exposure	1.94	1.39	2.72	1.87	1.34	2.61
Early and later exposure	2.12	1.53	2.93	1.99	1.44	2.77
<i>Disorders of the spine</i>						
No exposure	1			1		
Early exposure	1.88	1.03	3.43	1.76	0.96	3.22
Later exposure	2.48	1.49	4.14	2.40	1.41	4.06
Inconsistent exposure	2.31	1.34	3.98	2.30	1.34	3.95
Early and later exposure	2.61	1.55	4.39	2.43	1.42	4.14
<i>Upper extremity disorders</i>						
No exposure	1			1		
Early exposure	2.51	1.03	6.12	2.16	0.87	5.37
Later exposure	2.30	0.99	5.38	2.02	0.85	4.85
Inconsistent exposure	2.32	0.96	5.65	2.26	0.94	5.43
Early and later exposure	4.77	2.26	10.1	3.97	1.86	8.46

* Model 1 adjusted for age and sex

† Model 2 adjusted for age, sex, smoking, BMI, physical activity and parental occupational class

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



289x80mm (300 x 300 DPI)

1 STROBE Statement— Halonen JI et al. Exposure to heavy physical work from early to later
 2
 3 adulthood and primary health care visits due to musculoskeletal diseases in midlife: a register linked
 4
 5 study
 6
 7

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract SEE Abstract on p. 3 (b) Provide in the abstract an informative and balanced summary of what was done and what was found SEE p. 3
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported SEE p. 4
Objectives	3	State specific objectives, including any pre-specified hypotheses SEE p. 5
Methods		
Study design	4	Present key elements of study design early in the paper SEE p. 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection SEE pp. 5-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up SEE pp. 5-7 (b) For matched studies, give matching criteria and number of exposed and unexposed NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable SEE pp. 6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group SEE pp. 5-8
Bias	9	Describe any efforts to address potential sources of bias SEE p. 8 (covariate adjustments and alternative analysis method)
Study size	10	Explain how the study size was arrived at SEE p. 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why SEE pp. 5-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding SEE p. 8 (b) Describe any methods used to examine subgroups and interactions SEE p. 8 (c) Explain how missing data were addressed Missing data were imputed, see p. 7-8 (d) If applicable, explain how loss to follow-up was addressed NA (e) Describe any sensitivity analyses SEE p. 8
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed SEE p. 5 and Table 1 (b) Give reasons for non-participation at each stage NA (c) Consider use of a flow diagram No flow diagram, inclusion criteria explained on page 5

1	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders SEE pp. 8-9, Table 1
2			(b) Indicate number of participants with missing data for each variable of interest SEE Table 1.
3			(c) Summarise follow-up time (eg, average and total amount) see p. 8
4	Outcome data	15*	Report numbers of outcome events or summary measures over time SEE Table 2.
5	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included SEE Table 3
6			(b) Report category boundaries when continuous variables were categorized See pp. 5-7
7			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period NA
8	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses SEE p. 8
9	Discussion		
10	Key results	18	Summarise key results with reference to study objectives SEE p. 9
11	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias SEE pp. 10-11
12	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence SEE pp. 9-11
13	Generalizability	21	Discuss the generalizability (external validity) of the study results SEE p. 11
14	Other information		
15	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based SEE pp. 12-13

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

Exposure to heavy physical work from early to later adulthood and primary health care visits due to musculoskeletal diseases in midlife: a register linked study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-031564.R1
Article Type:	Research
Date Submitted by the Author:	04-Jul-2019
Complete List of Authors:	Halonen, Jaana; Finnish Institute of Occupational Health Shiri, Rahman; Finnish Institute of Occupational Health, Centre of Expertise for Health and Work Ability Mänty, Minna; University of Helsinki, Department of Public Health Sumanen, Hilla; South-Eastern Finland University of Applied Sciences, Health care and emergency care; University of Helsinki, Public Health Solovieva, Svetlana; Finnish Institute of Occupational Health, Center of Expertise for Health and workability Viikari-Juntura, Eira; Finnish Institute of Occupational Health, Kahonen, Mika; University of Tampere , Department of Clinical Physiology; Tampere University Hospital Lehtimäki, Terho Raitakari, Olli; University of Turku, Research Centre of Applied and Preventive Cardiovascular Medicine; Turku University Hospital, Department of Clinical Physiology and Nuclear Medicine Lallukka, Tea; Työterveyslaitos ; Helsingin Yliopisto Laaketieteellinen tiedekunta, Department of Public Health
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Epidemiology
Keywords:	Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, Physical work, Spine < ORTHOPAEDIC & TRAUMA SURGERY, Upper extremity, OCCUPATIONAL & INDUSTRIAL MEDICINE

SCHOLARONE™
Manuscripts

1
2
3 *Research article: BMJ Open*
4

5 Exposure to heavy physical work from early to later adulthood and primary
6 health care visits due to musculoskeletal diseases in midlife: a register linked
7
8 study
9
10
11
12

13 Jaana I. Halonen,¹ Rahman Shiri,¹ Minna Mänty,^{2,3} Hilla Sumanen,^{3,4} Svetlana Solovieva,¹

14 Eira Viikari-Juntura,¹ Mika Kähönen,⁵ Terho Lehtimäki,⁶ Olli T. Raitakari,^{7,8,9} Tea

15 Lallukka^{1,3}
16
17
18

19
20 1 Finnish Institute of Occupational Health, Helsinki, Finland
21

22 2 City of Vantaa, Finland
23

24 3 Department of Public Health, University of Helsinki, Helsinki, Finland
25

26 4 South-Eastern Finland University of Applied Sciences, Kotka, Finland
27

28 5 Department of Clinical Physiology, Tampere University Hospital, and Finnish
29 Cardiovascular Research Center - Tampere, Faculty of Medicine and Health Technology,
30 Tampere University, Tampere 33521, Finland
31

32 6 Department of Clinical Chemistry, Fimlab Laboratories, and Finnish Cardiovascular
33 Research Center - Tampere, Faculty of Medicine and Health Technology, Tampere
34 University, Tampere 33520, Finland
35

36 7 Centre for Population Health Research, University of Turku and Turku University Hospital,
37 Turku, Finland.
38

39 8 Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku,
40 Turku, Finland.
41

42 9 Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital,
43 Turku, Finland.
44

45
46
47
48
49
50 Corresponding author: Jaana I. Halonen, address: Finnish Institute of Occupational Health,
51 70032 TYÖTERVEYSLAITOS, Finland
52

53 E-mail: jaana.halonen@ttl.fi Telephone: +358 43 82 44 264
54

55
56
57 **Running title** Physical work from early to later adulthood and musculoskeletal visits
58

59 **Word count** 2784
60

Abstract (280/300)

Objectives: To examine whether exposure to heavy physical work from early to later adulthood is associated with primary health care visits due to cause-specific musculoskeletal diseases in midlife.

Design: Prospective cohort study

Setting: Nationally representative Young Finns Study cohort, Finland.

Participants: 1056 participants of the Young Finns Study cohort.

Exposure measure: Physical work exposure was surveyed in early (18–24 years old, 1986 or 1989) and later adulthood (2007 and 2011), and it was categorized as: “no exposure”, “early exposure only”, “later exposure only”, and “early and later exposure”.

Primary and secondary outcome measures: Visits due to any musculoskeletal disease and separately due to spine disorders, and upper extremity disorders were followed-up from national primary health care register from the date of the third survey in 2011 until 2014.

Results: Prevalence of any musculoskeletal disease during the follow-up was 20%, that for spine disorders 10%, and that for upper extremity disorders 5%. Those with physically heavy work in early adulthood only had an increased risk of any musculoskeletal disease (risk ratio (RR) 1.55, 95% confidence interval (CI) 1.05–2.28) after adjustment for age, sex, smoking, body mass index, physical activity, and parental occupational class. Later exposure only was associated with visits due to any musculoskeletal disease (RR 1.46, 95% CI 1.01–2.12) and spine disorders (RR 2.40, 95% CI 1.41–4.06). Early and later exposure was associated with all three outcomes: RRs 1.99 (95% CI 1.44–2.77) for any musculoskeletal disease, 2.43 (95% CI 1.42–4.14) for spine disorders, and 3.97 (95% CI 1.86–8.46) for upper extremity disorders.

1
2
3 **Conclusions:** To reduce burden of musculoskeletal diseases, preventive actions to reduce
4 exposure to or mitigate the consequences of physically heavy work throughout the work
5 career are needed.
6
7

8
9
10 **Key words:** musculoskeletal; physical work; spine disorder; upper extremity
11
12

13 14 15 **Strengths and limitations of this study**

- 16
17 • We used self-reported assessment of physical heaviness of work that was based on a
18 single question, which is why the specificity of the exposure, e.g. regarding exposure
19 of different parts of the body, is low.
20
21
- 22
23 • We cannot rule out the possibility of changes in the exposure or outcomes between
24 the survey waves.
25
26
- 27
28 • The setting enabled us to prospectively examine the long-term consequences of
29 exposure to early and later physical work and midlife musculoskeletal health
30 problems that were objectively measured.
31
32
- 33
34 • The used cohort data were representative of the general population with relatively
35 little loss to follow-up.
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Musculoskeletal diseases (MSD) are, along with mental disorders, the leading cause of work disability¹ measured as sickness absence² and disability retirements.³ In the European Union, the estimated total cost of lost productivity attributable to MSD among working-aged people can be up to 2% of gross domestic product (GDP).⁴ Contextual factors, particularly those related to workplace, have been identified as risk factors for sickness absence and disability retirement due to musculoskeletal problems^{5,6} as well as for musculoskeletal pain.⁷ We have reported findings where early and cumulative exposure to physical work were associated with low back pain at midlife.⁸ However, pain as an outcome is always self-reported, as well as a common condition. Thus, objective outcome measures are needed to confirm whether the effects of early and cumulative physical work are similar for more severe and objectively assessed MSD outcomes.

Only few studies to date have been able to assess the associations between cumulative exposure to physical work and MSD. A recent study used a job exposure matrix to assess exposure at the level of occupational title and disability retirement due to MSD,⁶ but even the first exposure measurements were mainly from midlife. In another study, two individual-level measurements were used to examine the associations between long-term exposure to high physical workload in midlife and risk of disability retirement due to MSD after age of 61,⁹ while younger employees were not included. Yet another study used individual-level physical work exposure data that were retrospectively assessed, and observed that cumulative exposure may increase the risk of sickness absence and disability retirement, but results for cause-specific outcomes were not reported.¹⁰ In addition to the lack of cumulative exposure data, prior studies have rarely accounted for family background although parental socioeconomic position has been linked, for example, to later

1
2
3 musculoskeletal problems¹¹ and widespread pain¹² as well as career possibilities¹³ and
4
5 choices.¹⁴
6

7
8 To fill these gaps in evidence, we examined whether physical heaviness of work
9
10 from early adulthood to later adulthood is associated with primary health care visits due to
11
12 MSD in midlife. We hypothesized that early, later and repeated exposure to heavy work is
13
14 associated with later health care visits. Any MSD was examined as one outcome group, but
15
16 we also included two cause-specific groups: disorders of the spine and upper extremities. The
17
18 contribution of behavioural factors and parental socioeconomic position in these associations
19
20 were considered.
21
22
23
24
25

26 **Methods**

27 **Participants**

28
29 Data for this study are derived from the Young Finns Study.¹⁵ Cohort baseline data were
30
31 collected in 1980 in six age strata: 3, 6, 9, 12, 15, and 18 years resulting in 3596 participants
32
33 (response rate 83%). For this study, we included all those who were 18, 21 or 24 years when
34
35 responding to the survey in 1986 (early adulthood). These data were completed by including
36
37 also those who turned 18 years and responded to the survey in 1989 (**Figure 1**). The age-
38
39 based selection criterion was applied as the focus of this study was on early work-related
40
41 exposures. Further inclusion criterion required that the participants responded to the question
42
43 on physical heaviness of work in 1986 or 1989 (early adulthood exposure, N=1119), and in
44
45 2007 (later adulthood exposure, N=1090) and/or in 2011 (later adulthood exposure, N=1042),
46
47 which resulted in a total of 10854 participants. After excluding those with missing data on
48
49 any covariate (after re-coding and imputation), the final study sample was 1056 cohort
50
51 participants (with 5171 observations) who all had work exposure measurement from early
52
53
54
55
56
57
58
59
60

1
2
3 adulthood and at least one measurement from later adulthood. The study has been ethically
4
5 approved by the Ethics Committee of the Hospital District of Southwest Finland.
6
7
8
9

10 Patient and Public Involvement statement

11
12 Patients or the public were not involved in the development of the research question or the
13
14 design of this study nor in the conduct of the study.
15
16
17

18 Exposure

19
20 Physical heaviness of work was enquired at waves 1 to 3 with a single question: “How heavy
21
22 is your work physically?”. There were six response alternatives: 1) light sedentary work, 2)
23
24 other sedentary work, 3) physically light work, involving standing and moving, 4) medium
25
26 heavy work involving moving, 5) physically heavy work, and 6) physically very heavy work.
27
28 The responses were categorized as: sedentary/physically light work, and medium to heavy
29
30 physical work. We used responses from all three waves to form a five-class exposure variable
31
32 categorized as: “no exposure”, when reporting sedentary/physically light work in all three
33
34 waves, “early exposure only”, when reporting medium to heavy physical work only in wave
35
36 1, “later exposure only”, when reporting medium to heavy physical work in waves 2 or 3
37
38 (89% responded to both waves 2 and 3), and “early and later exposure” when reporting
39
40 medium to heavy physical work in wave 1 and in later adulthood in wave 2 and/or 3. All
41
42 other possible response combinations formed a group “inconsistent exposure”.
43
44
45
46
47
48
49
50

51 Outcomes

52
53 We examined primary health care visits due to a musculoskeletal diagnosis. The follow-up
54
55 started from the day after returning wave 3 survey in 2011. Repeated visits were used for the
56
57 main analyses. For an alternative analysis, time to the first visit was used as an outcome, and
58
59
60

1
2
3 the follow-up from returning the survey in 2011 continued until the first primary health care
4 visit, death (from Statistics Finland) or end of the follow-up (end of 2014), whichever
5 occurred first. Data were obtained from the register of primary health care visits (Avohilmo)
6 maintained by National Institute for Health and Welfare.¹⁶ Diagnosis-specific data have been
7 collected and were available from 2011 onwards. Visits due to *any musculoskeletal diagnosis*
8 by International Classification of Diseases (ICD) version 10 codes M00-M99 were examined
9 over the follow-up period. Additionally, two cause-specific outcome groups with the largest
10 numbers of events were: 1) disorders of the spine and 2) upper extremity disorders. *Disorders*
11 *of the spine* included any of the following diseases, surgeries or treatments (ICD-10 code):
12 cervical disc disorders (M50), lumbar and other intervertebral disc disorders with
13 radiculopathy (M51.1), other specified intervertebral disc displacement (M51.2), disc
14 degeneration (M51.3), disc disorders (M51.8), intervertebral disc disorder, unspecified
15 (M51.9), disc disorder/ disc disease (back disorders with radiation: M50, M51), other
16 dorsopathies (M53), back pain / dorsalgia (back disorders without radiation: M54.1, M54.2,
17 M54.3, M54.4, M54.5, M54.6, M54.8, M54.9), and lumbar disc herniation or sciatica
18 (M51.1, M51.2, M54.3, and M54.4). *Upper extremity disorders* included any of the following
19 diseases, surgeries or treatments: carpal tunnel syndrome, carpal tunnel release (G56.0,
20 ACC51, ACC59), shoulder disorder (M75), medial epicondylitis, lateral epicondylitis, and
21 periarthritis of wrist (M77.0, M77.1, M77.2, or M77.3). Additionally, the numbers of visits
22 due to osteoarthritis (M15, M16, M17, M18) were examined, but found to be too low for
23 statistical analyses (see Table 1).

53 Covariates

54 From the questionnaires we obtained information on possible confounders. We included sex
55 and age at wave 1, and parental occupational status in childhood (1=upper non-manual,
56
57
58
59
60

1
2
3 2=lower non-manual, 3=upper manual, 4=lower manual). Smoking (ever smoker vs. non-
4
5 smoker) and body mass index (BMI, kg/m² based on measured weight and height) were
6
7 included as time varying covariates collected at baseline, 2001, 2007 and 2011. Measure for
8
9 leisure-time physical activity (PA) was based on a set of questions requesting the frequency
10
11 and intensity of PA, frequency of vigorous PA, hours spent on vigorous PA, average duration
12
13 of a PA session, and participation in organized PA. Based on these questions a *physical*
14
15 *activity index* was calculated (range 5-15, larger value indicating greater activity).¹⁷ For PA,
16
17 we used the maximum of the three measurements of the PA index in adulthood (2001, 2007
18
19 and 2011), as these data had plenty of missing values (N missing =730 in 2001, 150 in 2007
20
21 and 475 in 2011), but the patterns of PA have been observed to remain constant in
22
23 adulthood.¹⁸ Missing data on smoking were re-coded as “non-smoker”, and missing data on
24
25 BMI were imputed using mean of the study sample in the corresponding survey. Although
26
27 this is not the strongest imputation method we considered it was the most applicable one, as
28
29 the method only concerned one covariate. All these covariates have been linked to back
30
31 problems in prior studies^{11 19-21} and smoking can be also considered as an indicator of low
32
33 socioeconomic position, which may affect the choice of employment and further physical
34
35 workload.
36
37
38
39
40
41
42
43
44
45

46 Statistical analyses

47 We used generalized estimating equation (GEE) models with Poisson distribution to assess
48
49 associations between the five-class physical work exposure, “no exposure” serving as the
50
51 reference group, and repeated primary health care visits due to MSD. This method was
52
53 chosen as the GEE models permit specification of a working correlation matrix that accounts
54
55 for the form of within-subject correlation of responses on dependent variables of many
56
57 different distributions, including Poisson.²² We ran models separately for all musculoskeletal
58
59
60

1
2
3 visits, for disorders of the spine, and for upper extremity disorders. Two model specifications
4
5 were used: Model 1 was adjusted for sex and age at baseline, Model 2 was additionally
6
7 adjusted for parental occupational class, physical activity, and time-varying smoking and
8
9 BMI. Results are presented as risk ratios (RR) with 95% confidence intervals (CI). As an
10
11 alternative method, we ran the analyses using Cox proportional hazard models using time to
12
13 the first visit as the outcome, which resulted in very similar findings (supplemental Table 1).
14
15
16
17
18

19 **Results**

20
21 Descriptive statistics of the analysis sample in total and by sex are shown in Table 1. At
22
23 baseline, mean age was 20.5 (SD=2.9) years, and mean BMI 22.4 (SD=2.3), while the mean
24
25 BMI during the follow-up was 25.5 (SD=4.8). Mean follow-up time for first visits due to any
26
27 MSD was 3.2 (SD=0.87) years, due to spine disorders 3.4 (SD=0.63) years, and due to upper
28
29 extremity disorders 3.4 (SD=0.50) years. In the total sample, prevalence of any
30
31 musculoskeletal disease during the follow-up was 20%, that for spine disorders 10%, and that
32
33 for upper extremity disorders 5%. Distributions of the outcomes and proportions of events in
34
35 each of the five exposure groups in total and by sex are presented in Table 2. As shown in
36
37 Table 2, the low numbers of events prevented sex-specific analyses.
38
39
40
41

42 Associations between physical heaviness of work and primary health care visits
43
44 due to the three outcome groups are presented in Table 3. Overall, the age- and sex-adjusted
45
46 estimates (Model 1) were slightly attenuated after including parental occupational status
47
48 smoking, BMI and physical activity (Model 2). We observed an association between early
49
50 exposure only and any musculoskeletal disorders (fully adjusted RR 1.55, 95% CI 1.05–2.28)
51
52 and a slightly weaker association for later exposure only (RR 1.46, 95% 1.01–2.12). Early
53
54 and later exposure had the strongest association with any visits due to MSD (RR 1.99, 95%
55
56 CI 1.44–2.77).
57
58
59
60

1
2
3 For disorders of the spine, we observed an association for later exposure only
4 (RR 2.40, 95% CI 1.41–4.06), inconsistent exposure (RR 2.30, 95% CI 1.34–3.95), and early
5 and later exposure (RR 2.43, 95% CI 1.42–4.14). Effect estimates for visits due to upper
6 and later exposure (RR 2.43, 95% CI 1.42–4.14). Effect estimates for visits due to upper
7 extremity disorders were also positive, that for early and later exposure (HR 3.97, 95% CI
8 1.86–8.46) reaching statistical significance, although with a wide confidence interval.
9
10
11
12
13
14
15
16

17 Discussion

18
19 In this study, reporting both early and later exposure to heavy physical work was associated
20 with objectively measured MSDs requiring primary health care visit in midlife. In addition,
21 physical heaviness of work in early adulthood only was associated with an increased risk of
22 primary health care visit due to any MSD, and exposure in later adulthood only was
23 associated with any MSD and disorders of the spine. These diagnosis-specific findings are in
24 line with our prior findings for self-reported low back pain.⁸ Although our current analyses
25 may have lacked power to detect precise associations, particularly for upper extremity
26 disorders, the findings suggest that physical work exposure is also a predictor of objectively
27 measured MSDs even after considering behavioural factors and parental socioeconomic
28 position.
29
30
31
32
33
34
35
36
37
38
39
40
41

42 Longitudinal studies on the associations between physical work exposures and
43 objectively measured MSDs are scarce. Specifically, we are not aware of studies that would
44 have collected and used data on work-related physical exposures of participants from early to
45 later adulthood, and health care visits due to MSDs in midlife. Some evidence exists
46 regarding physical work exposures and musculoskeletal pain or disorders at an early stage of
47 the working career. In one cross-sectional study repetitive and asymmetric demands,
48 including high probability of repetitive tasks, bending or rotation movements and manual
49 materials handling, was associated with the presence of neck/shoulder pain and severity of
50
51
52
53
54
55
56
57
58
59
60

1
2
3 upper- and lower-back pain among 21-year-old employees.²³ Another cross-sectional study
4
5 among less than 30-year-old employees reported similar results regarding the association
6
7 between physical work exposures (e.g. repetitive flexion or rotation movements of the trunk,
8
9 and more than three years in a job including lifting more than 25 kg at least once an hour) and
10
11 low back pain.²⁴ However, in these studies follow-up for mid-life musculoskeletal disorders
12
13 was not available. Timing of outcome measurement seems essential as it is likely that there
14
15 are differences in associations between physical work and MSD among 20-35, 36-49 and
16
17 over 50-year old employees.²⁵

21
22 Several studies have reported associations between physical work exposures
23
24 and increased risk of objectively measured disability retirement due to MSD.^{5 26-28} However,
25
26 only one of these studies examined how exposure in early adulthood was associated with
27
28 disability retirement due to MSD in mid-life.²⁸ Moreover, only a few studies have reported
29
30 associations between cumulative exposure to physical work throughout the work career and
31
32 objectively measured sickness absence or disability retirement in general,²⁹ or due to
33
34 disability retirement due to MSD in particular.⁶ These findings have been in line with ours,
35
36 although the cumulative exposure in the study focusing on MSD was assessed using a job
37
38 exposure matrix.
39
40

42
43 Some limitations of this study need to be acknowledged. We used self-reported
44
45 assessment of physical heaviness of work that was based on a single question. Consequently,
46
47 the specificity of the exposure, e.g. regarding exposure of different parts of the body, is low.
48
49 Although such questions have widely been used in epidemiological studies and have
50
51 indicated good validity,³⁰ this may partly explain the non-significant associations between
52
53 physical work and upper extremity disorders. We also used a dichotomized physical
54
55 heaviness of work measure where medium and heavy/very heavy work were combined as the
56
57 proportion of those with heavy/very heavy work was rather low (10% at early adulthood).
58
59
60

1
2
3 The used cut-off may have attenuated the observed associations if medium heavy work had
4 substantially weaker association with health care visits than heavy/very heavy work. We
5 cannot rule out the possibility of changes in the exposure or outcomes between the survey
6 waves, which may have caused under- or over-estimation of the associations. However, the
7 long follow-up enabled us to examine the long-term consequences of early and later physical
8 work and midlife musculoskeletal health problems that were objectively measured. Some
9 healthy worker effect may have attenuated the findings as we required minimum of two
10 responses (from early and later adulthood) regarding physical heaviness of work and those
11 with physically strenuous work or with musculoskeletal problems may have left employment
12 before the second survey. It can also be speculated that primary health care visits with
13 musculoskeletal diagnosis in midlife are mostly a result of pain complaints. Severe pain may
14 interfere with work activities and induce need for sickness absence, which may be the
15 primary motivation for the visit to a physician. Thus, the used outcomes may reflect the
16 severity of work disability due to a subjective measure of musculoskeletal pain. The follow-
17 up period for the outcomes was not very long and unobserved changes in the exposure or
18 covariates during the outcome follow-up could have caused some bias to the findings
19 resulting in under- or overestimation of the observed associations. However, the major
20 strength of this work is the prospective study design with three repeated assessments of
21 physical heaviness of work that were initiated in early adulthood. Moreover, the used cohort
22 data were representative of the general population with relatively little loss to follow-up.¹⁵ As
23 we used register data, only persons who emigrate will no more have registered health care
24 visits. This suggests good generalizability to the Finnish working population, while more
25 caution is needed when assessing generalizability to other countries with different health care
26 systems.

1
2
3 In summary, our findings suggest that exposure to heavy physical work over the
4 work career contributes to the high burden in the health care. Therefore, preventive actions
5 against musculoskeletal problems due to physically heavy work in early adulthood, later
6 adulthood and cumulatively throughout the work career are needed. One possible action,
7 specifically among young employees, might be good introduction to ergonomic ways to
8 work. Guidance on how to recover from physical work tasks is also important; for example,
9 at individual level recovery training has been seen beneficial to the employees.³¹ At
10 organizational level, procedures enabling recovery during the work day could include task
11 variation and convenient work-break schedules,³¹ which are likely to be applicable
12 throughout the work career.
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

29 **A competing interest declaration**

30 All authors have completed the Unified Competing Interest form at
31 www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and
32 declare that (1) JIH and TLa have support from the Academy of Finland; (2) JIH and TLa
33 have no relationships with the Finnish Academy that might have an interest in the submitted
34 work in the previous 3 years; (3) their spouses, partners, or children have no financial
35 relationships that may be relevant to the submitted work; and (4) JIH, RS, HS, MM, SS, EV-
36 J, MK, TLe, OR and TLa have no non-financial interests that may be relevant to the
37 submitted work.
38
39
40
41
42
43
44
45
46
47
48
49
50

51 **Authors' contributions** JIH, RS, MM, HS, EV-J, SS and TLa conceived and designed the
52 experiments, TLa analysed the data, JIH wrote the first draft of the article, MK, TLe and OR
53 contributed materials and/or analysis tools. TLa, MK, TLe and OR contributed to the funding
54
55
56
57
58
59
60

1
2
3 of the study. TLa is the guarantor of the study. All authors were involved in interpretation of
4
5 the findings, writing the paper and approved the submitted and published versions.
6
7
8
9

10 **Funding** The research was funded by the Finnish Academy (grant numbers 287488 and
11
12 319200 for TLa and JIH). The Young Finns Study has been financially supported by the
13
14 Academy of Finland: grants 286284, 134309 (Eye), 126925, 121584, 124282, 129364,
15
16 129378 (Salve), 117787 (Gendi), and 41071 (Skidi); the Social Insurance Institution of
17
18 Finland; Competitive State Research Financing of the Expert Responsibility area of Kuopio,
19
20 Tampere and Turku University Hospitals (grant X51001); Juho Vainio Foundation; Paavo
21
22 Nurmi Foundation; Finnish Foundation for Cardiovascular Research; Finnish Cultural
23
24 Foundation; The Sigrid Juselius Foundation; Tampere Tuberculosis Foundation; Emil
25
26 Aaltonen Foundation; Yrjö Jahnsson Foundation; Signe and Ane Gyllenberg Foundation;
27
28 Diabetes Research Foundation of Finnish Diabetes Association; and EU Horizon 2020 (grant
29
30 755320 for TAXINOMISIS); and European Research Council (grant 742927 for
31
32 MULTIEPIGEN project); Tampere University Hospital Supporting Foundation.
33
34
35
36
37
38
39

40 **Ethics approval** The study has received ethical approval from the Ethics Committee of the
41
42 Hospital District of Southwest Finland on September 21st, 2010.
43
44
45
46

47 **Data sharing** TLa had access to an anonymized subset of the data that were used for the
48
49 analyses. OTR had full access to all raw data. Raw data from the study are not available due
50
51 to confidentiality and sensitivity issues. Subset of raw data can be requested from OTR
52
53 olli.raitakari[at]utu.fi.
54
55
56
57
58
59
60

1
2
3 **Acknowledgements** The authors thank statistician Niina Kartiosuo for her help with the
4
5 formation of the analysis dataset.
6
7
8
9

10 **Figure Legend**

11
12 **Figure 1.** Flow chart of the sample selection.
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

References

- 1 OECD. *Sickness, Disability and Work: Breaking the Barriers. A Synthesis of Findings across OECD Countries* OECD Publishing, Paris. 2010.
- 2 Linaker C, Harris EC, Cooper C, Coggon D, Palmer KT. The burden of sickness absence from musculoskeletal causes in Great Britain. *Occup Med (Lond)* 2011;61:458-64.
- 3 Statistics Finland. Recipients of disability pension 2018.
- 4 Bevan S. Economic impact of musculoskeletal disorders (MSDs) on work in Europe. *Best Pract Res Clin Rheumatol* 2015;29:356-73.
- 5 Foss L, Gravseth HM, Kristensen P et al. The impact of workplace risk factors on long-term musculoskeletal sickness absence: a registry-based 5-year follow-up from the Oslo health study. *J Occup Environ Med* 2011;53:1478-82.
- 6 Ervasti J, Pietilainen O, Rahkonen O et al. Long-term exposure to heavy physical work, disability pension due to musculoskeletal disorders and all-cause mortality: 20-year follow-up-introducing Helsinki Health Study job exposure matrix. *Int Arch Occup Environ Health* 2018.
- 7 Madsen IEH, Gupta N, Budtz-Jorgensen E et al. Physical work demands and psychosocial working conditions as predictors of musculoskeletal pain: a cohort study comparing self-reported and job exposure matrix measurements. *Occup Environ Med* 2018;75:752-758.
- 8 Lallukka T, Viikari-Juntura E, Viikari J et al. Early work-related physical exposures and low back pain in midlife: the Cardiovascular Risk in Young Finns Study. *Occup Environ Med* 2017;74:163-168.
- 9 Kjellberg K, Lundin A, Falkstedt D, Allebeck P, Hemmingsson T. Long-term physical workload in middle age and disability pension in men and women: a follow-up study of Swedish cohorts. *Int Arch Occup Environ Health* 2016;89:1239-1250.
- 10 Sundstrup E, Hansen AM, Mortensen EL et al. Retrospectively assessed physical work environment during working life and risk of sickness absence and labour market exit among older workers. *Occup Environ Med* 2018;75:114-123.
- 11 Lallukka T, Viikari-Juntura E, Raitakari OT et al. Childhood and adult socio-economic position and social mobility as determinants of low back pain outcomes. *Eur J Pain* 2014;18:128-38.
- 12 Power C, Atherton K, Strachan DP et al. Life-course influences on health in British adults: effects of socio-economic position in childhood and adulthood. *Int J Epidemiol* 2007;36:532-9.
- 13 Laukkonen M-L. Pienituloisten perheiden ylioppilaat välttävät riskiä pääsykokeita painottavissa opiskelijavalinnoissa [High school graduates from low income families evade risk related to student admission emphasizing entrance examinations]: ETLA 2018.
- 14 Whiston SC, Keller BK. The Influences of the Family of Origin on Career Development: A Review and Analysis. *The Counseling Psychologist* 2004;32:493-568.
- 15 Raitakari OT, Juonala M, Rönnemaa T et al. Cohort profile: the cardiovascular risk in Young Finns Study. *Int J Epidemiol* 2008;37:1220-6.
- 16 National Institute for Health and Welfare. Register of Primary Health Care visits, Helsinki: National Institute for Health and Welfare 2019.
- 17 Rovio SP, Yang X, Kankaanpää A et al. Longitudinal physical activity trajectories from childhood to adulthood and their determinants: The Young Finns Study. *Scand J Med Sci Sports* 2018;28:1073-1083.
- 18 Telama R, Yang X, Leskinen E et al. Tracking of physical activity from early childhood through youth into adulthood. *Med Sci Sports Exerc* 2014;46:955-62.
- 19 Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between smoking and low back pain: a meta-analysis. *Am J Med* 2010;123:87.e7-35.
- 20 -. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol* 2010;171:135-54.

- 1
2
3 21 Shiri R, Euro U, Heliövaara M et al. Lifestyle Risk Factors Increase the Risk of Hospitalization
4 for Sciatica: Findings of Four Prospective Cohort Studies. *Am J Med* 2017;130:1408-1414.e6.
5 22 Ballinger GA. Using Generalized Estimating Equations for Longitudinal Data Analysis.
6 *Organizational Research Methods* 2004;7:127-150.
7 23 Lourenco S, Araujo F, Severo M, Cunha Miranda L, Carnide F, Lucas R. Patterns of
8 biomechanical demands are associated with musculoskeletal pain in the beginning of
9 professional life: a population-based study. *Scand J Work Environ Health* 2015;41:234-46.
10 24 Van Nieuwenhuysse A, Fatkhutdinova L, Verbeke G et al. Risk factors for first-ever low back
11 pain among workers in their first employment. *Occup Med (Lond)* 2004;54:513-9.
12 25 Oakman J, Neupane S, Nygard CH. Does age matter in predicting musculoskeletal disorder
13 risk? An analysis of workplace predictors over 4 years. *Int Arch Occup Environ Health*
14 2016;89:1127-36.
15 26 Lahelma E, Laaksonen M, Lallukka T et al. Working conditions as risk factors for disability
16 retirement: a longitudinal register linkage study. *BMC Public Health* 2012;12:309.
17 27 Robroek SJW, Jarvholm B, van der Beek AJ, Proper KI, Wahlstrom J, Burdorf A. Influence of
18 obesity and physical workload on disability benefits among construction workers followed
19 up for 37 years. *Occup Environ Med* 2017;74:621-627.
20 28 Ropponen A, Svedberg P, Koskenvuo M, Silventoinen K, Kaprio J. Physical work load and
21 psychological stress of daily activities as predictors of disability pension due to
22 musculoskeletal disorders. *Scand J Public Health* 2014;42:370-6.
23 29 Sundstrup E, Hansen AM, Mortensen EL et al. Cumulative occupational mechanical
24 exposures during working life and risk of sickness absence and disability pension:
25 prospective cohort study. *Scand J Work Environ Health* 2017;43:415-425.
26 30 Stock SR, Fernandes R, Delisle A, Vezina N. Reproducibility and validity of workers' self-
27 reports of physical work demands. *Scand J Work Environ Health* 2005;31:409-37.
28 31 Verbeek J, Ruotsalainen J, Laitinen J et al. Interventions to enhance recovery in healthy
29 workers; a scoping review. *Occup Med (Lond)* 2018.
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1. Descriptive statistics of the study population at baseline.

Variable	All	
	N	%
Total individuals	1065	100
Women	446	42
Men	610	58
Parental occupational status		
upper non-manual	152	14
lower non-manual	447	42
upper manual	282	27
lower manual	175	17
Ever smokers	516	49
Low physical activity index*	710	67
Cumulative exposure to heavy physical work		
No exposure	523	49
Early exposure only	124	13
Later exposure only	130	12
Inconsistent exposure	118	11
Early and later exposure	161	15
Outcomes (-)		
Any musculoskeletal disease	221	21
Disorders of the spine	107	10
Upper extremity disorders	52	5
Osteoarthritis	16	1.5

* Index score 5-10

Table 2. Number of observations and proportions (%) of primary health care visits due to musculoskeletal diseases by the exposure categories for physical heaviness of work between 2011 and 2014.

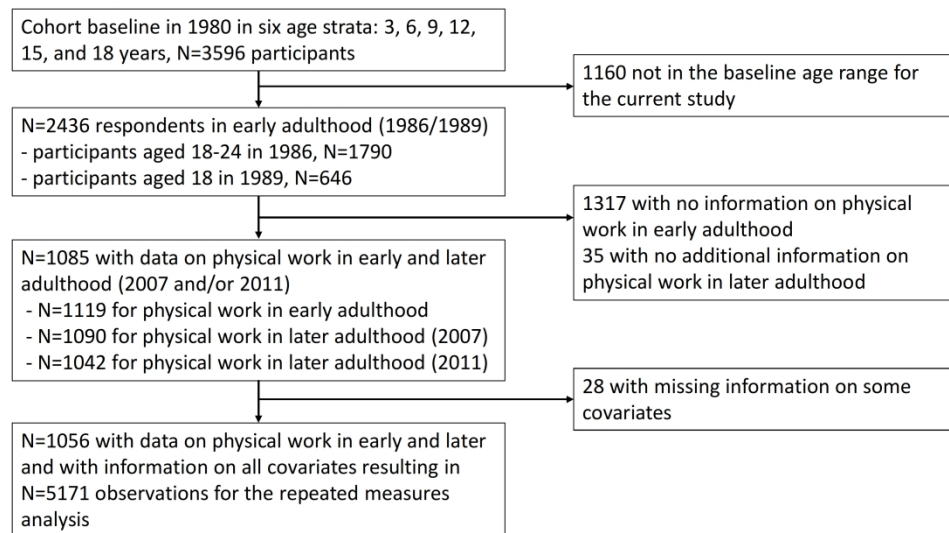
Physical heaviness of work	Any musculoskeletal disease N _{obs} (%)	Disorders of the spine N _{obs} (%)	Upper extremity disorders N _{obs} (%)	Osteoarthritis N _{obs} (%)
All	1083	527	253	79
No exposure	405 (37)	168 (32)	66 (26)	44 (56)
Early exposure	137 (13)	64 (12)	34 (13)	20 (25)
Later exposure	156 (14)	102 (19)	40 (16)	5 (6)
Inconsistent exposure	168 (16)	85 (16)	34 (13)	10 (13)
Early and later exposure	217 (20)	108 (21)	79 (31)	0 (0)
Women	730	353	165	59
No exposure	334 (46)	148 (42)	47 (28)	35 (58)
Early exposure	58 (8)	29 (8)	14 (8)	15 (25)
Later exposure	107 (15)	63 (18)	30 (18)	5 (8)
Inconsistent exposure	128 (18)	55 (16)	34 (21)	5 (8)
Early and later exposure	103 (14)	58 (16)	40 (24)	0 (0)
Men	353	174	88	20
No exposure	71 (20)	20 (11)	19 (22)	10 (50)
Early exposure	79 (22)	35 (20)	20 (23)	5 (25)
Later exposure	49 (14)	39 (23)	10 (11)	0 (0)
Inconsistent exposure	40 (11)	30 (17)	0 (0)	5 (25)
Early and later exposure	115 (32)	50 (29)	39 (44)	0 (0)

Table 3. Risk ratios for primary health care visits due to musculoskeletal diseases in relation to early and later exposure to heavy physical work.

Physical heaviness of work	Model 1*			Model 2†		
	RR	95% CI		RR	95% CI	
<i>Any musculoskeletal disease</i>						
No exposure	1			1		
Early exposure	1.65	1.12	2.41	1.55	1.05	2.28
Later exposure	1.57	1.09	2.24	1.46	1.01	2.12
Inconsistent exposure	1.90	1.35	2.67	1.87	1.34	2.61
Early and later exposure	2.14	1.55	2.97	1.99	1.44	2.77
<i>Disorders of the spine</i>						
No exposure	1			1		
Early exposure	1.87	1.02	3.42	1.76	0.96	3.22
Later exposure	2.51	1.51	4.18	2.40	1.41	4.06
Inconsistent exposure	2.32	1.35	3.99	2.30	1.34	3.95
Early and later exposure	2.62	1.56	4.40	2.43	1.42	4.14
<i>Upper extremity disorders</i>						
No exposure	1			1		
Early exposure	2.50	1.03	6.11	2.16	0.87	5.37
Later exposure	2.33	1.00	5.67	2.02	0.85	4.85
Inconsistent exposure	2.33	0.96	5.67	2.26	0.94	5.43
Early and later exposure	4.79	2.28	10.1	3.97	1.86	8.46

* Model 1 adjusted for age and sex

† Model 2 adjusted for age, sex, smoking, BMI, physical activity and parental occupational class



25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. Flow chart of the sample selection.

1
2
3 **Supplemental material**
4
5
6
7

8 Exposure to heavy physical work from early to later adulthood and primary
9
10 health care visits due to musculoskeletal diseases in midlife: a register linked
11
12
13 study
14

15
16 Jaana I. Halonen, Rahman Shiri, Minna Mänty, Hilla Sumanen, Svetlana Solovieva, Eira
17 Viikari-Juntura, Mika Kähönen, Terho Lehtimäki, Olli T. Raitakari, Tea Lallukka
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplemental Table 1. Associations between early and later exposure to heavy physical work and primary health care visits due to musculoskeletal diseases from Cox proportional hazard models.

Physical heaviness of work	Model 1*			Model 2†		
	HR	95% CI		HR	95% CI	
<i>Any musculoskeletal disease</i>						
No exposure	1			1		
Early exposure	1.95	1.22	3.11	1.90	1.18	3.06
Later exposure	1.36	0.84	2.22	1.32	0.81	2.16
Inconsistent exposure	2.01	1.27	3.17	2.01	1.27	3.17
Early and later exposure	2.41	1.56	3.73	2.26	1.45	3.52
<i>Disorders of the spine</i>						
No exposure	1			1		
Early exposure	2.43	1.17	5.05	2.37	1.14	4.95
Later exposure	2.54	1.30	4.96	2.48	1.26	4.88
Inconsistent exposure	2.36	1.15	4.85	2.38	1.15	4.89
Early and later exposure	3.51	1.81	6.83	3.29	1.67	6.48
<i>Upper extremity disorders</i>						
No exposure	1			1		
Early exposure	3.75	1.28	11.0	3.38	1.14	10.1
Later exposure	2.48	0.80	7.64	2.22	0.72	6.87
Inconsistent exposure	2.46	0.74	8.17	2.27	0.68	7.62
Early and later exposure	6.12	2.33	16.0	4.84	1.81	12.9

* Model 1 adjusted for age and sex

† Model 2 adjusted for age, sex, smoking, BMI, and parental occupational class

1 STROBE Statement— Halonen JI et al. Exposure to heavy physical work from early to later
 2
 3 adulthood and primary health care visits due to musculoskeletal diseases in midlife: a register linked
 4
 5 study
 6
 7

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract SEE Abstract on p. 2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found SEE Abstract on p. 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported SEE p. 4
Objectives	3	State specific objectives, including any pre-specified hypotheses SEE p. 5
Methods		
Study design	4	Present key elements of study design early in the paper SEE p. 5 for description of the study cohort
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection SEE pp. 5-6 (setting), 6 (exposure), 6-7 (outcomes and follow-up)
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up SEE p. 5 (b) For matched studies, give matching criteria and number of exposed and unexposed NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable SEE pp. 6 (exposure), 6-7 (outcome), 8 (covariates)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group SEE pp. 5 (setting), 6 (exposure), 6-7 (outcomes), 8 (covariates)
Bias	9	Describe any efforts to address potential sources of bias SEE pp. 8-9 (covariate adjustments and alternative analysis method)
Study size	10	Explain how the study size was arrived at SEE p. 5 and Figure 1 (flow chart)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why SEE pp. 6 (exposure), 6-7 (outcomes), 8 (covariates)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding SEE pp. 8-9 (b) Describe any methods used to examine subgroups and interactions SEE pp. 8-9 (c) Explain how missing data were addressed SEE p. 8 (covariates) (d) If applicable, explain how loss to follow-up was addressed NA (e) Describe any sensitivity analyses SEE p. 9

Results

1	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed SEE p. 5 and Figure 1
2			(b) Give reasons for non-participation at each stage NA
3			(c) Consider use of a flow diagram Figure 1 is a flow diagram
4			
5			
6			
7	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders SEE p. 9 and Table 1
8			(b) Indicate number of participants with missing data for each variable of interest Those with missing data were excluded, see page 5 and Figure 1.
9			(c) Summarise follow-up time (eg, average and total amount) NA
10			
11	Outcome data	15*	Report numbers of outcome events or summary measures over time SEE Table 2.
12			
13	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included SEE Table 3
14			(b) Report category boundaries when continuous variables were categorized See pp. 6 (exposure), 8 (covariates)
15			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Unadjusted absolute risks provided in the abstract on page 2 and on page 9.
16			
17	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses SEE p. 9 and supplemental Table 1.
18			
19			
20			
21			
22			
23			
24			
25			
26			
27			
28	Discussion		
29	Key results	18	Summarise key results with reference to study objectives SEE p. 10
30			
31	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias SEE pp. 11-12
32			
33			
34	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence SEE p. 13
35			
36			
37			
38	Generalizability	21	Discuss the generalizability (external validity) of the study results SEE p. 12
39			
40	Other information		
41	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based SEE p. 14
42			
43			
44			

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

Exposure to heavy physical work from early to later adulthood and primary health care visits due to musculoskeletal diseases in midlife: a register linked study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-031564.R2
Article Type:	Research
Date Submitted by the Author:	06-Aug-2019
Complete List of Authors:	Halonen, Jaana; Finnish Institute of Occupational Health Shiri, Rahman; Finnish Institute of Occupational Health, Centre of Expertise for Health and Work Ability Mänty, Minna; University of Helsinki, Department of Public Health Sumanen, Hilla; South-Eastern Finland University of Applied Sciences, Health care and emergency care; University of Helsinki, Public Health Solovieva, Svetlana; Finnish Institute of Occupational Health, Center of Expertise for Health and workability Viikari-Juntura, Eira; Finnish Institute of Occupational Health, Kahonen, Mika; University of Tampere , Department of Clinical Physiology; Tampere University Hospital Lehtimäki, Terho Raitakari, Olli; University of Turku, Research Centre of Applied and Preventive Cardiovascular Medicine; Turku University Hospital, Department of Clinical Physiology and Nuclear Medicine Lallukka, Tea; Työterveyslaitos ; Helsingin Yliopisto Laaketieteellinen tiedekunta, Department of Public Health
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Epidemiology
Keywords:	Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, Physical work, Spine < ORTHOPAEDIC & TRAUMA SURGERY, Upper extremity, OCCUPATIONAL & INDUSTRIAL MEDICINE

SCHOLARONE™
Manuscripts

1
2
3 *Research article: BMJ Open*
4

5 Exposure to heavy physical work from early to later adulthood and primary
6 health care visits due to musculoskeletal diseases in midlife: a register linked
7
8 study
9
10
11
12

13 Jaana I. Halonen,¹ Rahman Shiri,¹ Minna Mänty,^{2,3} Hilla Sumanen,^{3,4} Svetlana Solovieva,¹

14 Eira Viikari-Juntura,¹ Mika Kähönen,⁵ Terho Lehtimäki,⁶ Olli T. Raitakari,^{7,8,9} Tea

15 Lallukka^{1,3}
16
17
18
19

20 1 Finnish Institute of Occupational Health, Helsinki, Finland

21 2 City of Vantaa, Finland

22 3 Department of Public Health, University of Helsinki, Helsinki, Finland

23 4 South-Eastern Finland University of Applied Sciences, Kotka, Finland

24 5 Department of Clinical Physiology, Tampere University Hospital, and Finnish
25 Cardiovascular Research Center - Tampere, Faculty of Medicine and Health Technology,
26 Tampere University, Tampere 33521, Finland

27 6 Department of Clinical Chemistry, Fimlab Laboratories, and Finnish Cardiovascular
28 Research Center - Tampere, Faculty of Medicine and Health Technology, Tampere
29 University, Tampere 33520, Finland

30 7 Centre for Population Health Research, University of Turku and Turku University Hospital,
31 Turku, Finland.

32 8 Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku,
33 Turku, Finland.

34 9 Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital,
35 Turku, Finland.
36
37
38
39
40

41 Corresponding author: Jaana I. Halonen, address: Finnish Institute of Occupational Health,
42 70032 TYÖTERVEYSLAITOS, Finland
43
44

45 E-mail: jaana.halonen@ttl.fi Telephone: +358 43 82 44 264
46
47
48
49

50 **Running title** Physical work from early to later adulthood and musculoskeletal visits
51
52

53 **Word count** 2834
54
55
56
57
58
59
60

Abstract (280/300)

Objectives: To examine whether exposure to heavy physical work from early to later adulthood is associated with primary health care visits due to cause-specific musculoskeletal diseases in midlife.

Design: Prospective cohort study

Setting: Nationally representative Young Finns Study cohort, Finland.

Participants: 1056 participants of the Young Finns Study cohort.

Exposure measure: Physical work exposure was surveyed in early (18–24 years old, 1986 or 1989) and later adulthood (2007 and 2011), and it was categorized as: “no exposure”, “early exposure only”, “later exposure only”, and “early and later exposure”.

Primary and secondary outcome measures: Visits due to any musculoskeletal disease and separately due to spine disorders, and upper extremity disorders were followed-up from national primary health care register from the date of the third survey in 2011 until 2014.

Results: Prevalence of any musculoskeletal disease during the follow-up was 20%, that for spine disorders 10%, and that for upper extremity disorders 5%. Those with physically heavy work in early adulthood only had an increased risk of any musculoskeletal disease (risk ratio (RR) 1.55, 95% confidence interval (CI) 1.05–2.28) after adjustment for age, sex, smoking, body mass index, physical activity, and parental occupational class. Later exposure only was associated with visits due to any musculoskeletal disease (RR 1.46, 95% CI 1.01–2.12) and spine disorders (RR 2.40, 95% CI 1.41–4.06). Early and later exposure was associated with all three outcomes: RRs 1.99 (95% CI 1.44–2.77) for any musculoskeletal disease, 2.43 (95% CI 1.42–4.14) for spine disorders, and 3.97 (95% CI 1.86–8.46) for upper extremity disorders.

1
2
3 **Conclusions:** To reduce burden of musculoskeletal diseases, preventive actions to reduce
4 exposure to or mitigate the consequences of physically heavy work throughout the work
5 career are needed.
6
7

8
9
10 **Key words:** musculoskeletal; physical work; spine disorder; upper extremity
11
12

13 14 **Strengths and limitations of this study**

- 15
16
17 • We used self-reported assessment of physical heaviness of work that was based on a
18 single question, which is why the specificity of the exposure, e.g. regarding exposure
19 of different parts of the body, is low.
20
21
- 22
23
24 • We cannot rule out the possibility of changes in the exposure or outcomes between
25 the survey waves.
26
27
- 28
29
30 • The setting enabled us to prospectively examine the long-term consequences of
31 exposure to early and later physical work and midlife musculoskeletal health
32 problems that were objectively measured.
33
34
- 35
36
37 • The used cohort data were representative of the general population with relatively
38 little loss to follow-up.
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Musculoskeletal diseases (MSD) are, along with mental disorders, the leading cause of work disability¹ measured as sickness absence² and disability retirements.³ In the European Union, the estimated total cost of lost productivity attributable to MSD among working-aged people can be up to 2% of gross domestic product (GDP).⁴ Contextual factors, particularly those related to workplace, have been identified as risk factors for sickness absence and disability retirement due to musculoskeletal problems^{5,6} as well as for musculoskeletal pain.⁷ We have reported findings where early and cumulative exposure to physical work were associated with low back pain at midlife.⁸ However, pain as an outcome is always self-reported, as well as a common condition. Thus, objective outcome measures are needed to confirm whether the effects of early and cumulative physical work are similar for more severe and objectively assessed MSD outcomes.

Only few studies to date have been able to assess the associations between cumulative exposure to physical work and MSD. A recent study used a job exposure matrix to assess exposure at the level of occupational title and disability retirement due to MSD,⁶ but even the first exposure measurements were mainly from midlife. In another study, two individual-level measurements were used to examine the associations between long-term exposure to high physical workload in midlife and risk of disability retirement due to MSD after age of 61,⁹ while younger employees were not included. Yet another study used individual-level physical work exposure data that were retrospectively assessed, and observed that cumulative exposure may increase the risk of sickness absence and disability retirement, but results for cause-specific outcomes were not reported.¹⁰ In addition to the lack of cumulative exposure data, prior studies have rarely accounted for family background although parental socioeconomic position has been linked, for example, to later

1
2
3 musculoskeletal problems¹¹ and widespread pain¹² as well as career possibilities¹³ and
4
5 choices.¹⁴
6

7
8 To fill these gaps in evidence, we examined whether physical heaviness of work
9
10 from early adulthood to later adulthood is associated with primary health care visits due to
11
12 MSD in midlife. We hypothesized that early, later and repeated exposure to heavy work is
13
14 associated with later health care visits. Any MSD was examined as one outcome group, but
15
16 we also included two cause-specific groups: disorders of the spine and upper extremities. The
17
18 contribution of behavioural factors and parental socioeconomic position in these associations
19
20 were considered.
21
22
23
24
25

26 **Methods**

27 **Participants**

28
29 Data for this study are derived from the Young Finns Study.¹⁵ Cohort baseline data were
30
31 collected in 1980 in six age strata: 3, 6, 9, 12, 15, and 18 years resulting in 3596 participants
32
33 (response rate 83%). For this study, we included all those who were 18, 21 or 24 years when
34
35 responding to the survey in 1986 (early adulthood). These data were completed by including
36
37 also those who turned 18 years and responded to the survey in 1989 (**Figure 1**). The age-
38
39 based selection criterion was applied as the focus of this study was on early work-related
40
41 exposures. Further inclusion criterion required that the participants responded to the question
42
43 on physical heaviness of work in 1986 or 1989 (early adulthood exposure, N=1119), and in
44
45 2007 (later adulthood exposure, N=1090) and/or in 2011 (later adulthood exposure, N=1042),
46
47 which resulted in a total of 10854 participants. After excluding those with missing data on
48
49 any covariate (after re-coding and imputation), the final study sample was 1056 cohort
50
51 participants (with 5171 observations) who all had work exposure measurement from early
52
53
54
55
56
57
58
59
60

1
2
3 adulthood and at least one measurement from later adulthood. The study has been ethically
4
5 approved by the Ethics Committee of the Hospital District of Southwest Finland.
6
7
8
9

10 Patient and Public Involvement statement

11
12 Patients or the public were not involved in the development of the research question or the
13
14 design of this study nor in the conduct of the study.
15
16
17

18 Exposure

19
20 Physical heaviness of work was enquired at waves 1 to 3 with a single question: “How heavy
21
22 is your work physically?”. There were six response alternatives: 1) light sedentary work, 2)
23
24 other sedentary work, 3) physically light work, involving standing and moving, 4) medium
25
26 heavy work involving moving, 5) physically heavy work, and 6) physically very heavy work.
27
28 The responses were categorized as: sedentary/physically light work, and medium to heavy
29
30 physical work. We used responses from all three waves to form a five-class exposure variable
31
32 categorized as: “no exposure”, when reporting sedentary/physically light work in all three
33
34 waves, “early exposure only”, when reporting medium to heavy physical work only in wave
35
36 1, “later exposure only”, when reporting medium to heavy physical work in waves 2 or 3
37
38 (89% responded to both waves 2 and 3), and “early and later exposure” when reporting
39
40 medium to heavy physical work in wave 1 and in later adulthood in wave 2 and/or 3. All
41
42 other possible response combinations formed a group “inconsistent exposure”.
43
44
45
46
47
48
49
50

51 Outcomes

52
53 We examined primary health care visits due to a musculoskeletal diagnosis. The follow-up
54
55 started from the day after returning wave 3 survey in 2011. Repeated visits were used for the
56
57 main analyses. For an alternative analysis, time to the first visit was used as an outcome, and
58
59
60

1
2
3 the follow-up from returning the survey in 2011 continued until the first primary health care
4 visit, death (from Statistics Finland) or end of the follow-up (end of 2014), whichever
5 occurred first. Data were obtained from the register of primary health care visits (Avohilmo)
6 maintained by National Institute for Health and Welfare.¹⁶ Diagnosis-specific data have been
7 collected and were available from 2011 onwards. Visits due to *any musculoskeletal diagnosis*
8 by International Classification of Diseases (ICD) version 10 codes M00-M99 were examined
9 over the follow-up period. Additionally, two cause-specific outcome groups with the largest
10 numbers of events were: 1) disorders of the spine and 2) upper extremity disorders. *Disorders*
11 *of the spine* included any of the following diseases, surgeries or treatments (ICD-10 code):
12 cervical disc disorders (M50), lumbar and other intervertebral disc disorders with
13 radiculopathy (M51.1), other specified intervertebral disc displacement (M51.2), disc
14 degeneration (M51.3), disc disorders (M51.8), intervertebral disc disorder, unspecified
15 (M51.9), disc disorder/ disc disease (back disorders with radiation: M50, M51), other
16 dorsopathies (M53), back pain / dorsalgia (back disorders without radiation: M54.1, M54.2,
17 M54.3, M54.4, M54.5, M54.6, M54.8, M54.9), and lumbar disc herniation or sciatica
18 (M51.1, M51.2, M54.3, and M54.4). *Upper extremity disorders* included any of the following
19 diseases, surgeries or treatments: carpal tunnel syndrome, carpal tunnel release (G56.0,
20 ACC51, ACC59), shoulder disorder (M75), medial epicondylitis, lateral epicondylitis, and
21 periarthritis of wrist (M77.0, M77.1, M77.2, or M77.3). Additionally, the numbers of visits
22 due to osteoarthritis (M15, M16, M17, M18) were examined, but found to be too low for
23 statistical analyses (see Table 1).

53 Covariates

54 From the questionnaires we obtained information on possible confounders. We included sex
55 and age at wave 1, and parental occupational status in childhood (1=upper non-manual,
56
57
58
59
60

1
2
3 2=lower non-manual, 3=upper manual, 4=lower manual). Smoking (ever smoker vs. non-
4
5 smoker) and body mass index (BMI, kg/m² based on measured weight and height) were
6
7 included as time varying covariates collected at baseline, 2001, 2007 and 2011. Measure for
8
9 leisure-time physical activity (PA) was based on a set of questions requesting the frequency
10
11 and intensity of PA, frequency of vigorous PA, hours spent on vigorous PA, average duration
12
13 of a PA session, and participation in organized PA. Based on these questions a *physical*
14
15 *activity index* was calculated (range 5-15, larger value indicating greater activity).¹⁷ For PA,
16
17 we used the maximum of the three measurements of the PA index in adulthood (2001, 2007
18
19 and 2011), as these data had plenty of missing values (N missing =730 in 2001, 150 in 2007
20
21 and 475 in 2011), but the patterns of PA have been observed to remain constant in
22
23 adulthood.¹⁸ Missing data on smoking were re-coded as “non-smoker”. Number of missing
24
25 observations varied by phase from 5 in 2007 to 369 in 1986, some of which were excluded
26
27 due to missing data on other covariates. Missing data on BMI were imputed using mean of
28
29 the study sample in the corresponding survey. Number of missing observations varied from 0
30
31 in 2001 to 411 in 1989, some of which were excluded due to missing data on other
32
33 covariates. Although this is not the strongest imputation method we considered it was the
34
35 most applicable one, as the method only concerned one covariate. All these covariates have
36
37 been linked to back problems in prior studies^{11 19-21} and smoking can be also considered as an
38
39 indicator of low socioeconomic position, which may affect the choice of employment and
40
41 further physical workload.
42
43
44
45
46
47
48
49
50

51 Statistical analyses

52
53 We used generalized estimating equation (GEE) models with Poisson distribution to assess
54
55 associations between the five-class physical work exposure, “no exposure” serving as the
56
57 reference group, and repeated primary health care visits due to MSD. This method was
58
59
60

1
2
3 chosen as the GEE models permit specification of a working correlation matrix that accounts
4
5 for the form of within-subject correlation of responses on dependent variables of many
6
7 different distributions, including Poisson.²² We ran models separately for all musculoskeletal
8
9 visits, for disorders of the spine, and for upper extremity disorders. Two model specifications
10
11 were used: Model 1 was adjusted for sex and age at baseline, Model 2 was additionally
12
13 adjusted for parental occupational class, physical activity, and time-varying smoking and
14
15 BMI. Results are presented as risk ratios (RR) with 95% confidence intervals (CI). As an
16
17 alternative method, we ran the analyses using Cox proportional hazard models using time to
18
19 the first visit as the outcome, which resulted in very similar findings (supplemental Table 1).
20
21
22
23
24
25

26 **Results**

27
28 Descriptive statistics of the analysis sample in total and by sex are shown in Table 1. At
29
30 baseline, mean age was 20.5 (SD=2.9) years, and mean BMI 22.4 (SD=2.3), while the mean
31
32 BMI during the follow-up was 25.5 (SD=4.8). Mean follow-up time for first visits due to any
33
34 MSD was 3.2 (SD=0.87) years, due to spine disorders 3.4 (SD=0.63) years, and due to upper
35
36 extremity disorders 3.4 (SD=0.50) years. In the total sample, prevalence of any
37
38 musculoskeletal disease during the follow-up was 20%, that for spine disorders 10%, and that
39
40 for upper extremity disorders 5%. Distributions of the outcomes and proportions of events in
41
42 each of the five exposure groups in total and by sex are presented in Table 2. As shown in
43
44 Table 2, the low numbers of events prevented sex-specific analyses.
45
46
47
48

49 Associations between physical heaviness of work and primary health care visits
50
51 due to the three outcome groups are presented in Table 3. Overall, the age- and sex-adjusted
52
53 estimates (Model 1) were slightly attenuated after including parental occupational status
54
55 smoking, BMI and physical activity (Model 2). We observed an association between early
56
57 exposure only and any musculoskeletal disorders (fully adjusted RR 1.55, 95% CI 1.05–2.28)
58
59
60

1
2
3 and a slightly weaker association for later exposure only (RR 1.46, 95% 1.01–2.12). Early
4
5 and later exposure had the strongest association with any visits due to MSD (RR 1.99, 95%
6
7 CI 1.44–2.77).
8
9

10 For disorders of the spine, we observed an association for later exposure only
11
12 (RR 2.40, 95% CI 1.41–4.06), inconsistent exposure (RR 2.30, 95% CI 1.34–3.95), and early
13
14 and later exposure (RR 2.43, 95% CI 1.42–4.14). Effect estimates for visits due to upper
15
16 extremity disorders were also positive, that for early and later exposure (HR 3.97, 95% CI
17
18 1.86–8.46) reaching statistical significance, although with a wide confidence interval.
19
20
21
22
23

24 Discussion

25
26 In this study, reporting both early and later exposure to heavy physical work was associated
27
28 with objectively measured MSDs requiring primary health care visit in midlife. In addition,
29
30 physical heaviness of work in early adulthood only was associated with an increased risk of
31
32 primary health care visit due to any MSD, and exposure in later adulthood only was
33
34 associated with any MSD and disorders of the spine. These diagnosis-specific findings are in
35
36 line with our prior findings for self-reported low back pain.⁸ Although our current analyses
37
38 may have lacked power to detect precise associations, particularly for upper extremity
39
40 disorders, the findings suggest that physical work exposure is also a predictor of objectively
41
42 measured MSDs even after considering behavioural factors and parental socioeconomic
43
44 position.
45
46
47
48

49 Longitudinal studies on the associations between physical work exposures and
50
51 objectively measured MSDs are scarce. Specifically, we are not aware of studies that would
52
53 have collected and used data on work-related physical exposures of participants from early to
54
55 later adulthood, and health care visits due to MSDs in midlife. Some evidence exists
56
57 regarding physical work exposures and musculoskeletal pain or disorders at an early stage of
58
59
60

1
2
3 the working career. In one cross-sectional study repetitive and asymmetric demands,
4 including high probability of repetitive tasks, bending or rotation movements and manual
5 materials handling, was associated with the presence of neck/shoulder pain and severity of
6 upper- and lower-back pain among 21-year-old employees.²³ Another cross-sectional study
7 among less than 30-year-old employees reported similar results regarding the association
8 between physical work exposures (e.g. repetitive flexion or rotation movements of the trunk,
9 and more than three years in a job including lifting more than 25 kg at least once an hour) and
10 low back pain.²⁴ However, in these studies follow-up for mid-life musculoskeletal disorders
11 was not available. Timing of outcome measurement seems essential as it is likely that there
12 are differences in associations between physical work and MSD among 20-35, 36-49 and
13 over 50-year old employees.²⁵

14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Several studies have reported associations between physical work exposures and increased risk of objectively measured disability retirement due to MSD.^{5 26-28} However, only one of these studies examined how exposure in early adulthood was associated with disability retirement due to MSD in mid-life.²⁸ Moreover, only a few studies have reported associations between cumulative exposure to physical work throughout the work career and objectively measured sickness absence or disability retirement in general,²⁹ or due to disability retirement due to MSD in particular.⁶ These findings have been in line with ours, although the cumulative exposure in the study focusing on MSD was assessed using a job exposure matrix.

Some limitations of this study need to be acknowledged. We used self-reported assessment of physical heaviness of work that was based on a single question. Consequently, the specificity of the exposure, e.g. regarding exposure of different parts of the body, is low. Although such questions have widely been used in epidemiological studies and have indicated good validity,³⁰ this may partly explain the non-significant associations between

1
2
3 physical work and upper extremity disorders. We also used a dichotomized physical
4
5 heaviness of work measure where medium and heavy/very heavy work were combined as the
6
7 proportion of those with heavy/very heavy work was rather low (10% at early adulthood).
8
9 The used cut-off may have attenuated the observed associations if medium heavy work had
10
11 substantially weaker association with health care visits than heavy/very heavy work. We
12
13 cannot rule out the possibility of changes in the exposure or outcomes between the survey
14
15 waves, which may have caused under- or over-estimation of the associations. However, the
16
17 long follow-up enabled us to examine the long-term consequences of early and later physical
18
19 work and midlife musculoskeletal health problems that were objectively measured. Some
20
21 healthy worker effect may have attenuated the findings as we required minimum of two
22
23 responses (from early and later adulthood) regarding physical heaviness of work and those
24
25 with physically strenuous work or with musculoskeletal problems may have left employment
26
27 before the second survey. It can also be speculated that primary health care visits with
28
29 musculoskeletal diagnosis in midlife are mostly a result of pain complaints. Severe pain may
30
31 interfere with work activities and induce need for sickness absence, which may be the
32
33 primary motivation for the visit to a physician. Thus, the used outcomes may reflect the
34
35 severity of work disability due to a subjective measure of musculoskeletal pain. The follow-
36
37 up period for the outcomes was not very long and unobserved changes in the exposure or
38
39 covariates during the outcome follow-up could have caused some bias to the findings
40
41 resulting in under- or overestimation of the observed associations. However, the major
42
43 strength of this work is the prospective study design with three repeated assessments of
44
45 physical heaviness of work that were initiated in early adulthood. Moreover, the used cohort
46
47 data were representative of the general population with relatively little loss to follow-up.¹⁵ As
48
49 we used register data, only persons who emigrate will no more have registered health care
50
51 visits. This suggests good generalizability to the Finnish working population, while more
52
53
54
55
56
57
58
59
60

1
2
3 caution is needed when assessing generalizability to other countries with different health care
4
5 systems.
6

7
8 In summary, our findings suggest that exposure to heavy physical work over the
9
10 work career contributes to the high burden in the health care. Therefore, preventive actions
11
12 against musculoskeletal problems due to physically heavy work in early adulthood, later
13
14 adulthood and cumulatively throughout the work career are needed. One possible action,
15
16 specifically among young employees, might be good introduction to ergonomic ways to
17
18 work. Guidance on how to recover from physical work tasks is also important; for example,
19
20 at individual level recovery training has been seen beneficial to the employees.³¹ At
21
22 organizational level, procedures enabling recovery during the work day could include task
23
24 variation and convenient work-break schedules,³¹ which are likely to be applicable
25
26 throughout the work career.
27
28
29
30
31

32 33 **A competing interest declaration**

34
35 All authors have completed the Unified Competing Interest form at
36
37 www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and
38
39 declare that (1) JIH and TLa have support from the Academy of Finland; (2) JIH and TLa
40
41 have no relationships with the Finnish Academy that might have an interest in the submitted
42
43 work in the previous 3 years; (3) their spouses, partners, or children have no financial
44
45 relationships that may be relevant to the submitted work; and (4) JIH, RS, HS, MM, SS, EV-
46
47 J, MK, TLe, OR and TLa have no non-financial interests that may be relevant to the
48
49 submitted work.
50
51
52
53
54
55

56 **Authors' contributions** JIH, RS, MM, HS, EV-J, SS and TLa conceived and designed the
57
58 experiments, TLa analysed the data, JIH wrote the first draft of the article, MK, TLe and OR
59
60

1
2
3 contributed materials and/or analysis tools. TLa, MK, TLe and OR contributed to the funding
4
5 of the study. TLa is the guarantor of the study. All authors were involved in interpretation of
6
7 the findings, writing the paper and approved the submitted and published versions.
8
9

10
11
12 **Funding** The research was funded by the Finnish Academy (grant numbers 287488 and
13
14 319200 for TLa and JIH). The Young Finns Study has been financially supported by the
15
16 Academy of Finland: grants 286284, 134309 (Eye), 126925, 121584, 124282, 129364,
17
18 129378 (Salve), 117787 (Gendi), and 41071 (Skidi); the Social Insurance Institution of
19
20 Finland; Competitive State Research Financing of the Expert Responsibility area of Kuopio,
21
22 Tampere and Turku University Hospitals (grant X51001); Juho Vainio Foundation; Paavo
23
24 Nurmi Foundation; Finnish Foundation for Cardiovascular Research; Finnish Cultural
25
26 Foundation; The Sigrid Juselius Foundation; Tampere Tuberculosis Foundation; Emil
27
28 Aaltonen Foundation; Yrjö Jahnsson Foundation; Signe and Ane Gyllenberg Foundation;
29
30 Diabetes Research Foundation of Finnish Diabetes Association; and EU Horizon 2020 (grant
31
32 755320 for TAXINOMISIS); and European Research Council (grant 742927 for
33
34 MULTIEPIGEN project); Tampere University Hospital Supporting Foundation.
35
36
37
38
39
40
41

42 **Ethics approval** The study has received ethical approval from the Ethics Committee of the
43
44 Hospital District of Southwest Finland on September 21st, 2010.
45
46
47
48

49 **Data sharing** TLa had access to an anonymized subset of the data that were used for the
50
51 analyses. OTR had full access to all raw data. Raw data from the study are not available due
52
53 to confidentiality and sensitivity issues. Subset of raw data can be requested from OTR
54
55 olli.raitakari[at]utu.fi.
56
57
58
59
60

1
2
3 **Acknowledgements** The authors thank statistician Niina Kartiosuo for her help with the
4
5 formation of the analysis dataset.
6
7
8
9

10 **Figure Legend**

11
12 **Figure 1.** Flow chart of the sample selection.
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

References

- 1 OECD. *Sickness, Disability and Work: Breaking the Barriers. A Synthesis of Findings across OECD Countries* OECD Publishing, Paris. 2010.
- 2 Linaker C, Harris EC, Cooper C, Coggon D, Palmer KT. The burden of sickness absence from musculoskeletal causes in Great Britain. *Occup Med (Lond)* 2011;61:458-64.
- 3 Statistics Finland. Recipients of disability pension 2018.
- 4 Bevan S. Economic impact of musculoskeletal disorders (MSDs) on work in Europe. *Best Pract Res Clin Rheumatol* 2015;29:356-73.
- 5 Foss L, Gravseth HM, Kristensen P et al. The impact of workplace risk factors on long-term musculoskeletal sickness absence: a registry-based 5-year follow-up from the Oslo health study. *J Occup Environ Med* 2011;53:1478-82.
- 6 Ervasti J, Pietilainen O, Rahkonen O et al. Long-term exposure to heavy physical work, disability pension due to musculoskeletal disorders and all-cause mortality: 20-year follow-up-introducing Helsinki Health Study job exposure matrix. *Int Arch Occup Environ Health* 2018.
- 7 Madsen IEH, Gupta N, Budtz-Jorgensen E et al. Physical work demands and psychosocial working conditions as predictors of musculoskeletal pain: a cohort study comparing self-reported and job exposure matrix measurements. *Occup Environ Med* 2018;75:752-758.
- 8 Lallukka T, Viikari-Juntura E, Viikari J et al. Early work-related physical exposures and low back pain in midlife: the Cardiovascular Risk in Young Finns Study. *Occup Environ Med* 2017;74:163-168.
- 9 Kjellberg K, Lundin A, Falkstedt D, Allebeck P, Hemmingsson T. Long-term physical workload in middle age and disability pension in men and women: a follow-up study of Swedish cohorts. *Int Arch Occup Environ Health* 2016;89:1239-1250.
- 10 Sundstrup E, Hansen AM, Mortensen EL et al. Retrospectively assessed physical work environment during working life and risk of sickness absence and labour market exit among older workers. *Occup Environ Med* 2018;75:114-123.
- 11 Lallukka T, Viikari-Juntura E, Raitakari OT et al. Childhood and adult socio-economic position and social mobility as determinants of low back pain outcomes. *Eur J Pain* 2014;18:128-38.
- 12 Power C, Atherton K, Strachan DP et al. Life-course influences on health in British adults: effects of socio-economic position in childhood and adulthood. *Int J Epidemiol* 2007;36:532-9.
- 13 Laukkonen M-L. Pienituloisten perheiden ylioppilaat välttävät riskiä pääsykokeita painottavissa opiskelijavalinnoissa [High school graduates from low income families evade risk related to student admission emphasizing entrance examinations]: ETLA 2018.
- 14 Whiston SC, Keller BK. The Influences of the Family of Origin on Career Development: A Review and Analysis. *The Counseling Psychologist* 2004;32:493-568.
- 15 Raitakari OT, Juonala M, Rönnemaa T et al. Cohort profile: the cardiovascular risk in Young Finns Study. *Int J Epidemiol* 2008;37:1220-6.
- 16 National Institute for Health and Welfare. Register of Primary Health Care visits, Helsinki: National Institute for Health and Welfare 2019.
- 17 Rovio SP, Yang X, Kankaanpää A et al. Longitudinal physical activity trajectories from childhood to adulthood and their determinants: The Young Finns Study. *Scand J Med Sci Sports* 2018;28:1073-1083.
- 18 Telama R, Yang X, Leskinen E et al. Tracking of physical activity from early childhood through youth into adulthood. *Med Sci Sports Exerc* 2014;46:955-62.
- 19 Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between smoking and low back pain: a meta-analysis. *Am J Med* 2010;123:87.e7-35.
- 20 -. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol* 2010;171:135-54.

- 1
2
3 21 Shiri R, Euro U, Heliövaara M et al. Lifestyle Risk Factors Increase the Risk of Hospitalization
4 for Sciatica: Findings of Four Prospective Cohort Studies. *Am J Med* 2017;130:1408-1414.e6.
5 22 Ballinger GA. Using Generalized Estimating Equations for Longitudinal Data Analysis.
6 *Organizational Research Methods* 2004;7:127-150.
7 23 Lourenco S, Araujo F, Severo M, Cunha Miranda L, Carnide F, Lucas R. Patterns of
8 biomechanical demands are associated with musculoskeletal pain in the beginning of
9 professional life: a population-based study. *Scand J Work Environ Health* 2015;41:234-46.
10 24 Van Nieuwenhuysse A, Fatkhutdinova L, Verbeke G et al. Risk factors for first-ever low back
11 pain among workers in their first employment. *Occup Med (Lond)* 2004;54:513-9.
12 25 Oakman J, Neupane S, Nygard CH. Does age matter in predicting musculoskeletal disorder
13 risk? An analysis of workplace predictors over 4 years. *Int Arch Occup Environ Health*
14 2016;89:1127-36.
15 26 Lahelma E, Laaksonen M, Lallukka T et al. Working conditions as risk factors for disability
16 retirement: a longitudinal register linkage study. *BMC Public Health* 2012;12:309.
17 27 Robroek SJW, Jarvholm B, van der Beek AJ, Proper KI, Wahlstrom J, Burdorf A. Influence of
18 obesity and physical workload on disability benefits among construction workers followed
19 up for 37 years. *Occup Environ Med* 2017;74:621-627.
20 28 Ropponen A, Svedberg P, Koskenvuo M, Silventoinen K, Kaprio J. Physical work load and
21 psychological stress of daily activities as predictors of disability pension due to
22 musculoskeletal disorders. *Scand J Public Health* 2014;42:370-6.
23 29 Sundstrup E, Hansen AM, Mortensen EL et al. Cumulative occupational mechanical
24 exposures during working life and risk of sickness absence and disability pension:
25 prospective cohort study. *Scand J Work Environ Health* 2017;43:415-425.
26 30 Stock SR, Fernandes R, Delisle A, Vezina N. Reproducibility and validity of workers' self-
27 reports of physical work demands. *Scand J Work Environ Health* 2005;31:409-37.
28 31 Verbeek J, Ruotsalainen J, Laitinen J et al. Interventions to enhance recovery in healthy
29 workers; a scoping review. *Occup Med (Lond)* 2018.
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1. Descriptive statistics of the study population at baseline.

Variable	All	
	N	%
Total individuals	1065	100
Women	446	42
Men	610	58
Parental occupational status		
upper non-manual	152	14
lower non-manual	447	42
upper manual	282	27
lower manual	175	17
Ever smokers	516	49
Low physical activity index*	710	67
Cumulative exposure to heavy physical work		
No exposure	523	49
Early exposure only	124	13
Later exposure only	130	12
Inconsistent exposure	118	11
Early and later exposure	161	15
Outcomes (-)		
Any musculoskeletal disease	221	21
Disorders of the spine	107	10
Upper extremity disorders	52	5
Osteoarthritis	16	1.5

* Index score 5-10

Table 2. Number of observations and proportions (%) of primary health care visits due to musculoskeletal diseases by the exposure categories for physical heaviness of work between 2011 and 2014.

Physical heaviness of work	Any musculoskeletal disease N _{obs} (%)	Disorders of the spine N _{obs} (%)	Upper extremity disorders N _{obs} (%)	Osteoarthritis N _{obs} (%)
All	1083	527	253	79
No exposure	405 (37)	168 (32)	66 (26)	44 (56)
Early exposure	137 (13)	64 (12)	34 (13)	20 (25)
Later exposure	156 (14)	102 (19)	40 (16)	5 (6)
Inconsistent exposure	168 (16)	85 (16)	34 (13)	10 (13)
Early and later exposure	217 (20)	108 (21)	79 (31)	0 (0)
Women	730	353	165	59
No exposure	334 (46)	148 (42)	47 (28)	35 (58)
Early exposure	58 (8)	29 (8)	14 (8)	15 (25)
Later exposure	107 (15)	63 (18)	30 (18)	5 (8)
Inconsistent exposure	128 (18)	55 (16)	34 (21)	5 (8)
Early and later exposure	103 (14)	58 (16)	40 (24)	0 (0)
Men	353	174	88	20
No exposure	71 (20)	20 (11)	19 (22)	10 (50)
Early exposure	79 (22)	35 (20)	20 (23)	5 (25)
Later exposure	49 (14)	39 (23)	10 (11)	0 (0)
Inconsistent exposure	40 (11)	30 (17)	0 (0)	5 (25)
Early and later exposure	115 (32)	50 (29)	39 (44)	0 (0)

Table 3. Risk ratios for primary health care visits due to musculoskeletal diseases in relation to early and later exposure to heavy physical work.

Physical heaviness of work	Model 1*			Model 2†		
	RR	95% CI		RR	95% CI	
<i>Any musculoskeletal disease</i>						
No exposure	1			1		
Early exposure	1.65	1.12	2.41	1.55	1.05	2.28
Later exposure	1.57	1.09	2.24	1.46	1.01	2.12
Inconsistent exposure	1.90	1.35	2.67	1.87	1.34	2.61
Early and later exposure	2.14	1.55	2.97	1.99	1.44	2.77
<i>Disorders of the spine</i>						
No exposure	1			1		
Early exposure	1.87	1.02	3.42	1.76	0.96	3.22
Later exposure	2.51	1.51	4.18	2.40	1.41	4.06
Inconsistent exposure	2.32	1.35	3.99	2.30	1.34	3.95
Early and later exposure	2.62	1.56	4.40	2.43	1.42	4.14
<i>Upper extremity disorders</i>						
No exposure	1			1		
Early exposure	2.50	1.03	6.11	2.16	0.87	5.37
Later exposure	2.33	1.00	5.67	2.02	0.85	4.85
Inconsistent exposure	2.33	0.96	5.67	2.26	0.94	5.43
Early and later exposure	4.79	2.28	10.1	3.97	1.86	8.46

* Model 1 adjusted for age and sex

† Model 2 adjusted for age, sex, smoking, BMI, physical activity and parental occupational class

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

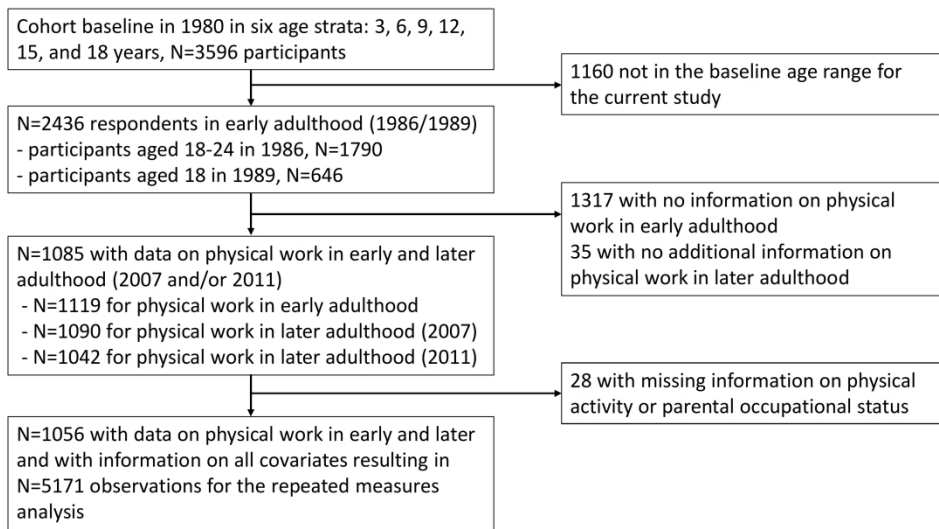


Figure 1. Flow chart of the sample selection.

1
2
3 **Supplemental material**
4
5
6
7

8 Exposure to heavy physical work from early to later adulthood and primary
9
10 health care visits due to musculoskeletal diseases in midlife: a register linked
11
12
13 study
14

15
16 Jaana I. Halonen, Rahman Shiri, Minna Mänty, Hilla Sumanen, Svetlana Solovieva, Eira
17 Viikari-Juntura, Mika Kähönen, Terho Lehtimäki, Olli T. Raitakari, Tea Lallukka
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplemental Table 1. Associations between early and later exposure to heavy physical work and primary health care visits due to musculoskeletal diseases from Cox proportional hazard models.

Physical heaviness of work	Model 1*			Model 2†		
	HR	95% CI		HR	95% CI	
<i>Any musculoskeletal disease</i>						
No exposure	1			1		
Early exposure	1.95	1.22	3.11	1.90	1.18	3.06
Later exposure	1.36	0.84	2.22	1.32	0.81	2.16
Inconsistent exposure	2.01	1.27	3.17	2.01	1.27	3.17
Early and later exposure	2.41	1.56	3.73	2.26	1.45	3.52
<i>Disorders of the spine</i>						
No exposure	1			1		
Early exposure	2.43	1.17	5.05	2.37	1.14	4.95
Later exposure	2.54	1.30	4.96	2.48	1.26	4.88
Inconsistent exposure	2.36	1.15	4.85	2.38	1.15	4.89
Early and later exposure	3.51	1.81	6.83	3.29	1.67	6.48
<i>Upper extremity disorders</i>						
No exposure	1			1		
Early exposure	3.75	1.28	11.0	3.38	1.14	10.1
Later exposure	2.48	0.80	7.64	2.22	0.72	6.87
Inconsistent exposure	2.46	0.74	8.17	2.27	0.68	7.62
Early and later exposure	6.12	2.33	16.0	4.84	1.81	12.9

* Model 1 adjusted for age and sex

† Model 2 adjusted for age, sex, smoking, BMI, and parental occupational class

1 STROBE Statement— Halonen JI et al. Exposure to heavy physical work from early to later
 2
 3 adulthood and primary health care visits due to musculoskeletal diseases in midlife: a register linked
 4
 5 study
 6
 7

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract SEE Abstract on p. 2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found SEE Abstract on p. 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported SEE p. 4
Objectives	3	State specific objectives, including any pre-specified hypotheses SEE p. 5
Methods		
Study design	4	Present key elements of study design early in the paper SEE p. 5 for description of the study cohort
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection SEE pp. 5-6 (setting), 6 (exposure), 6-7 (outcomes and follow-up)
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up SEE p. 5 (b) For matched studies, give matching criteria and number of exposed and unexposed NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable SEE pp. 6 (exposure), 6-7 (outcome), 8 (covariates)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group SEE pp. 5 (setting), 6 (exposure), 6-7 (outcomes), 8 (covariates)
Bias	9	Describe any efforts to address potential sources of bias SEE pp. 8-9 (covariate adjustments and alternative analysis method)
Study size	10	Explain how the study size was arrived at SEE p. 5 and Figure 1 (flow chart)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why SEE pp. 6 (exposure), 6-7 (outcomes), 8 (covariates)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding SEE pp. 8-9 (b) Describe any methods used to examine subgroups and interactions SEE pp. 8-9 (c) Explain how missing data were addressed SEE p. 8 (covariates) (d) If applicable, explain how loss to follow-up was addressed NA (e) Describe any sensitivity analyses SEE p. 9

Results

1	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed SEE p. 5 and Figure 1
2			(b) Give reasons for non-participation at each stage NA
3			(c) Consider use of a flow diagram Figure 1 is a flow diagram
4			
5			
6			
7	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders SEE p. 9 and Table 1
8			(b) Indicate number of participants with missing data for each variable of interest Those with missing data were excluded, see page 5 and Figure 1.
9			(c) Summarise follow-up time (eg, average and total amount) NA
10			
11			
12			
13			
14	Outcome data	15*	Report numbers of outcome events or summary measures over time SEE Table 2.
15	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included SEE Table 3
16			(b) Report category boundaries when continuous variables were categorized See pp. 6 (exposure), 8 (covariates)
17			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Unadjusted absolute risks provided in the abstract on page 2 and on page 9.
18			
19			
20			
21			
22			
23			
24			
25	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses SEE p. 9 and supplemental Table 1.
26			
27			
28	Discussion		
29	Key results	18	Summarise key results with reference to study objectives SEE p. 10
30	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias SEE pp. 11-12
31			
32			
33			
34	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence SEE p. 13
35			
36			
37			
38	Generalizability	21	Discuss the generalizability (external validity) of the study results SEE p. 12
39			
40	Other information		
41	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based SEE p. 14
42			
43			
44			

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.